A study of family history, deprivation and comorbidity in colorectal cancer

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Thank you to my sons Andrew and Greg, during the past year whilst writing this thesis they made it easy for me to take time out required.

Roseanne

Declaration

I herby declare,

(i) That this thesis was composed by myself

(ii) That the work presented within this thesis is my own , unless otherwise stated

(iii) That this work has not been submitted for any other degree or professional qualification

Signed .. .. Date 17TH MARCH 2005

Roseanne Cetnarskyj

March 2005

Abstract

A prospective study of 1540 colorectal cancer cases aged 16-79, diagnosed in Scotland between 3rd January 2002 and 31st December 2003 was conducted.

Aims

The main aims are:

Report the number and proportion of cases that perceive they have a family history risk of colorectal cancer.

Compare waiting time with symptoms and behaviour after development of symptoms, between cases that perceive a family history risk and do not perceive a family history risk.

Report the number and proportion of cases in this cohort with a family history of colorectal cancer that meet Scottish clinical criteria for high or moderate family history risk.

A secondary aim is:

Describe the average delay time in symptom presentation and the factors contributing to delay in presentation of lower gastrointestinal symptoms among cases with colorectal cancer and in particular assess the importance of deprivation and comorbidity.

Results

The distribution of sex and age at diagnosis were similar to other published population-based colorectal cancer studies. Of the 1540 cases, 222 (14.9%) cases perceived they had a family history of colorectal cancer.

280 (18.2%) cases out of 1540 were at a high or moderate family history risk according to Scottish Executive Guidelines. Of these 280 cases, 133 (47.5%) perceived they had a family history of colorectal cancer. Of these 133 cases, only 51 (18.2%) discussed this concern with their GP and, only 12 (4.3%) were referred to cancer genetic services.

Cases that perceived a family history risk of colorectal cancer were more likely to state they have knowledge of colorectal cancer symptoms and more likely to think that the lower gastrointestinal symptoms they develop are symptoms of colorectal cancer. However, this knowledge does not

prompt them to visit the GP with less delay after development of symptoms than those cases with no perception of a family history risk of colorectal cancer.

There was no association found between deprivation, comorbidity and timing of presentation following development of symptoms.

The more deprived group of patients were significantly more likely to report no knowledge of colorectal cancer symptoms. They were also less likely not to inspect the toilet or the toilet paper before flushing.

Implications for Health service

Providing all health professionals with the knowledge and skills to take a family history and to follow published guidelines when assessing family history risk would share the responsibility for identification of individuals with a high or moderate family, improve the appropriateness of referrals and reduce the inequality in access to cancer genetic services. It is estimated from this study that each year there will be 49 families in the colorectal cancer population at high risk eligible for mismatch repair gene analysis and 196 of their first-degree relatives that require two-yearly colonoscopy. In addition there will be 446 at moderate risk and eligible for microsatellite testing and 1784 first-degree relatives of these cases that require a colonoscopy at age 35 and 55 years.

The most deprived group of patients have the least knowledge of colorectal cancer symptoms and the design of educational material should acknowledge this fact and ensure that it is appropriate for this audience.

Conclusion

GPs do not appear to routinely use published guidelines to assess the family history of cases with colorectal cancer. The most affluent group are more likely to be aware that family history is a risk factor for colorectal cancer and those that discuss their concern of family history risk are more

likely to be referred to cancer genetic services. These findings suggest that inequality in access to the cancer genetic services exists.

Individuals in Scotland, that perceive a family history of colorectal cancer are not prompted by the development of lower gastrointestinal symptoms to visit their GP more quickly, nor does this knowledge change their behaviour in discussing symptoms with other people, self–treating symptoms, inspecting the toilet and toilet paper before flushing, even though they are more likely to perceive that they have colorectal cancer before visiting their GP.

There appears to be little differences in presentation and development of lower gastrointestinal symptoms or association with comorbidity between the most affluent and most deprived groups suggesting that socioeconomic status and comorbidity have little effect on behaviour after development of lower gastrointestinal symptoms.

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Foreword

Personal introduction

I have been employed as a genetic nurse specialist since 1997 and have a major research interest in cancer genetics and the development of cancer genetic practice. I have had several papers published from these research projects see *(Appendices 1-5)*.

Prior to this PhD research study, my main previous research experience has been in colorectal cancer. I recruited cases diagnosed with colorectal cancer (under the age of 55) to the Colorectal Cancer Genetic Susceptibility study (COGS), commenced in 1999. I was also the lead nurse in a three-year research study, the findings which led to the current clinical service model implemented in SE Scotland for individuals with a family history of cancer. I gained further relevant research experience during another community-based cancer genetic research project. In this study many individuals with colorectal cancer and their immediate family were seen for family history consultations. In parallel to this research experience, as genetic nurse specialist, I have my own weekly nurse led cancer genetic clinic. I have continued to deliver these clinics throughout the period of research leading to this PhD.

In all cases each consultand or study recruit had a detailed family history taken. It appeared to me that socioeconomic status might contribute to the understanding of the consultand's own family history risk and whether they discussed this perceived risk with their GP. Through my own experience and hearing the experiences of my colleagues I concluded that very few individuals with colorectal cancer were ever referred to the service, the majority of referrals being unaffected relatives of colorectal cancer cases. Recent changes in cancer genetic services have led to mutation analysis and gene testing

being available for some families; however, this is only available when there is DNA from an individual with colorectal cancer.

Prior to embarking on this PhD my colorectal cancer research experience was limited in a number of ways: the number of cases seen, the restricted age of cases seen (predominantly less than 55 years of age at diagnosis) and the geographical area was restricted to South East Scotland.

In defining the scope for my research I chose to focus on two main areas:

1. Family history and perceived family history risk, discussion of perceived family history with GP, family history risk (as assigned by established clinical guidelines) that are identified by the GP and referral patterns to cancer genetic services.
2. The timing of presentation with lower gastrointestinal symptoms to a GP and association between comorbidity or deprivation and the effect they may have on the waiting time with these symptoms before visiting a GP.

I was awarded a three-year research training fellowship from the Chief Scientist Office at the Scottish Executive, which commenced in January 2001. During this fellowship the research for this thesis was undertaken. Limited research has been published on family history risk of colorectal cancer cases as assigned by established clinical guidelines, perceived family history risk and referral of the cases with high and moderate family history risk to the cancer genetic services.

A family history of colorectal cancer is a known risk factor for developing colorectal cancer and referral guidelines to assist GPs in making a referral to cancer genetic services have recently been published and disseminated.

There is wide published literature on presentation patterns of individuals with lower gastrointestinal symptoms that are suspicious of colorectal cancer. Little research has been published on the association of comorbidity and deprivation after a diagnosis of colorectal cancer or the effect of comorbidity and deprivation on the reporting of symptoms.

There are no large population based studies of colorectal cancer in Scotland that have reported on symptom presentation associated with comorbidity and relationship to deprivation.

My role in this research study

I trained a team of research nurses to recruit and collect the data for this study. I personally recruited 5% of the cases. Recruitment took place as part of the Study of Colorectal Cancer in Scotland (SOCCS).

My contribution to this study is as follows:

- Development of the case information sheet and consent forms for MREC ethics application.
- Production and delivery of training programme for research nurses for the SOCCS study.
- Visits to each Scottish hospital to ensure that key staff where aware of the study, (by delivery of a presentation or personally meeting key staff).

- Development of standard operating procedures for recruitment in each hospital.
- Production of recruitment policies and data recording forms for all data collection in the SOCCS study.
- Development of the following data collection tools:
    - The symptom interview,
    - Ethnicity and ancestry questions in the SOCCS Cancer and Lifestyle questionnaire,
    - The medical data extraction form
    - The comorbidity form for recording data relevant to the comorbidity index.
- Appointment and the ongoing training of research nurses, reappointment and training of nursing positions throughout the time of the study.
- Provision of additional training and supervision required by staff recruiting to COGS study.
- Appointment of medical students and training of nurses and medical students to extract information from medical notes.
- Liaison in all hospitals with audit and medical records departments to monitor ascertainment and for the medical students and research nurses to gain access to medical notes.
- Ongoing management of research nursing team. This was achieved by one to one supervision of all nurses and regular nurse team meetings.
- Monitoring of recruitment in each hospital and problem solving in any hospital where access to eligible cases was difficult or recruitment appeared to be below the expected numbers.

- Completion of the genetic risk assessment on all family histories and writing a risk letter to cases assigned to have at moderate or high-risk family history (using Scottish guidelines).
- Overseeing the development of data scanning and data checking with the administrative team.

It was key to the collection of good quality data that the nursing team were well trained, offered ongoing support throughout the study and encouraged to undertake a research academic module and a cancer genetic module to enhance their knowledge and skills. I undertook this management and mentoring role of the research nurses in this study.

Data Collection

The data collection for this study was within a large DNA sample collection (*see methodology).*

Family history

A research nurse collected family history information in a face-to-face interview at recruitment. The pedigree was drawn on a standard family history form and a minimum of three generations was recorded.

Symptom interview

The symptom data was collected using a structured interview. The family history information and symptom interview was completed by the SOCCS research nurses throughout Scotland, as follows: Sheena Ross, Alison Ogilvie, Lisa McAuley, Daniela Rae, Jackie Kerrigan, Eleanor Russell, Janet Chauhan, Sheila Slater, Pamela Dalrymple,

Lisa Ferguson, Jenny Rodgers, Catherine Johnstone, Derek Baker, Tracey Millar, Louise McKenna, Karen Delahunty, Elaine Pagan and Isobel Williams.

Medical records

The information from medical notes was extracted either by the research nurses in the smaller hospitals or by the following trained medical students in the larger city hospitals; Lisa Massie, Jennifer Browning, Lois Tait, Yen Lim, Rachel Gardner, Chloe Keane, Kerry Hunter, Asma Kamal, Lynda Guthrie, Suzanne Price, and Sherry Zaman.

Data Entry

Family history

The family history was recorded on the standard form used by South East of Scotland cancer genetic service. I assessed the family history risk using published Scottish guidelines and risk entered on to a database by Maureen Edwards or Christine Thompson.

Symptom interview

I initially designed the final symptom interview using Microsoft Word and it was then translated using Teleform software package into a Teleform by Maureen Edwards this form could then be recognised by the Teleform reader when scanned. I checked all symptom interviews for errors, illegible handwriting and other items that might have caused problems with scanning. Dorothy Thompson carried out scanning of all symptom interviews. Dorothy Thompson and I carried out the checking of all scanned data entry via Teleform software.

Medical records and comorbidity form

I checked all completed medical records forms for missing data and other inaccuracies, prior to entry on database by Gisela Barr.

Pathology report

I confirmed that the case met eligibility criteria by reviewing the pathology reports when returned with medical records form.

Statistical analysis

Susan Holloway and Niall Anderson gave support with data analysis. Susan carried out power calculations and data analysis for the association of comorbidity and deprivation with symptoms waiting times. Niall developed the models for Cox Proportional Hazard modeling. I assisted in these analyses and independently carried out all other statistical tests in this thesis.

Chapter 1

Literature Search Methodology

Literature Search

Search strategy

The initial literature search for this study was completed during January 2001 and end of December 2001. The development of the research questions and data collection tools began after the initial literature search was complete. The literature searching continued throughout the data collection period and the writing of this thesis. During the data collection period some databases became obsolete or combined with other databases. All databases were searched on a regular basis for new publications using previously created search strategies. Some database providers offer a service to run your chosen search strategies and email the results on a regular basis. This service was activated when possible. In addition, requests were made to each relevant journal to have the table of contents emailed as they became available.

Literature Databases

The following databases were searched in the initial literature search:

- Medline from 1966
- Web of Science from 1981
- Cinhal from 1980
- CancerLit from 1975
- Embase from 1985
- Assia Plus from 1982
- Cochrane database from 1975

Where possible, database searches were limited to non-Medline references. Searches were limited to English abstracts and studies on humans. When it was possible duplicates were filtered from source.

Key areas and Keywords

The main key search topics in this thesis are family history, symptom presentation, comorbidity and deprivation. During this literature searching, all searches where carried out using keyword from each area and using the keywords colorectal, colon, rectal, bowel or colo–rectal and cancer, carcinoma or neoplasm (and all associated mesh headings).

The following is an expansion of relevant keywords for each area of study.

Family History

- Family history,
- Cancer family history,
- Risk assessment,
- Accuracy of family history,
- Family history guidelines,
- Family history criteria.

Symptom presentation

- Symptom presentation,
- Delay in symptom presentation,
- Delay in symptom or diagnosis,
- Symptom reporting,
- Duration of symptoms,
- Guidelines,
- Patient delay.

Comorbidity

- Comorbidity or co-morbidity,
- Concurrent disease,
- Comorbid disease or conditions.

Deprivation

- Socioeconomic or socio-economic,
- Socioeconomic or socio-economic status,
- Socioeconomic or socio-economic factors,
- Socioeconomic or socio-economic position,
- Socioeconomic or socio-economic environment,
- Deprivation,
- Inequalities,
- Material deprivation,
- Deprivation indices,
- Demographic factors,
- Social deprivation or class,
- Income inequality.

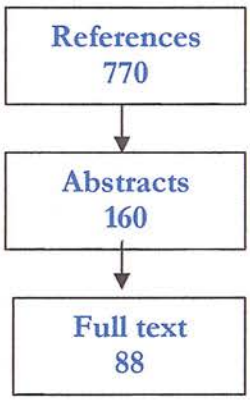
Within each search strategy all references were screened, when a paper appeared to be of relevance the abstract and references from that paper (if possible) were chosen and read.

One relevant paper with an English abstract but full text in Dutch was translated and referenced in this thesis.

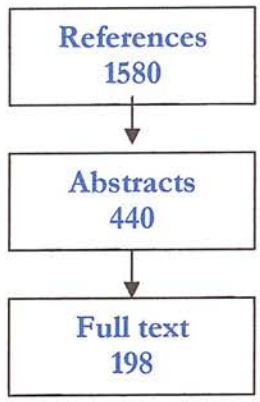
Literature search results

The following information is the numerical results of the initial literature search from January 2001 until end December 2001.

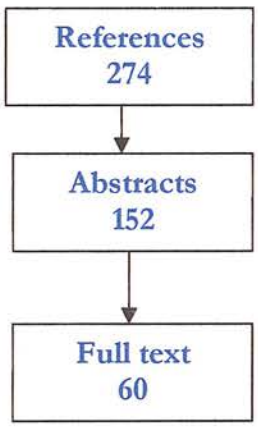
Family history



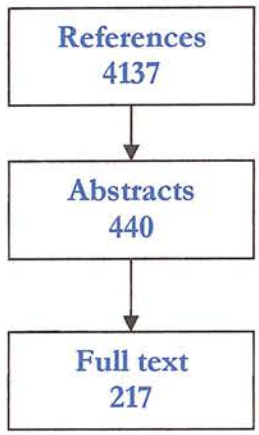
Symptom Presentation



Comorbidity



Deprivation



Secondary references

Many secondary references were sources from the reference list of a paper. The abstracts for these new references were read (if available) and when appropriate the full text was read, when no abstract was available full text was sourced. These main types of secondary references sourced from papers and included reports, editorials poster presentations and newsletter articles.

In addition to literature searching and secondary references as a source of evidence for this thesis, contact was made with a UK Colorectal Surgeon with a research interest in colorectal cancer symptoms. Contact was made with experts in Scotland if they had declared a research interest in the areas of deprivation and/or inequalities in health. Genetic units within UK were contacted for any unpublished information on ongoing family history studies. Following interactions with these experts, access was granted to a section of a thesis examined in London University, on 'colorectal cancer statistics in Scotland'. Two unpublished book chapters were received and permission to reference the material in this thesis was granted by one author, and a request not cited in my thesis, by the other. In addition, 2 unpublished papers were given but again confidentiality was requested. No material or data was received from genetic units; however the author is currently involved in a Scottish audit of breast, ovarian and colorectal cancer family history. Although the author could access these data, the data collection is not yet complete nor has any data cleaning been carried out.

Selection Criteria

Family history

Papers were chosen for reading when an abstract indicated that a study had included any form of family history criteria in the data collection. Also included, were papers that discussed the accuracy of family history data collection.

Symptom presentation

Papers were chosen for reading when an abstract indicated that the study had analysed data on presenting to a GP with any lower gastrointestinal symptoms. Also papers were selected when the abstract or titled mentioned use of guidelines.

Deprivation

Papers were chosen for reading when an abstract indicated that the study had a focus on any aspect of deprivation; non--Scottish studies were restricted to colorectal cancer included in a study. When Scottish studies indicated that aspects of deprivation were studied this was not restricted to colorectal cancer studies only but to any site of cancer.

Comorbidity

Papers were chosen for reading when an abstract indicated that studies were using any comorbidity index and related the use of the index to any cancer site.

Not all full text papers read were used in the final thesis.

Chapter 2

Introduction to Incidence of Colorectal Cancer

Colorectal cancer incidence

Colorectal cancer is principally a disease of economically developed populations. Low incidence is found throughout Central and South America, Asia and Africa. High incidence of colorectal cancer is found in Europe, Australia and North America. This high incidence has a major impact on health and use of health resources. The incidence of colorectal cancer increases with age and as the average life span for males and females is increasing the burden of disease from this condition increases accordingly.

Concerns regarding differences in incidence and survival throughout Europe led to the establishment of a collaborative project. In 1990, European cancer registries agreed to share data in the EUROCARE[1] project. EUROCARE-3 now has 76 participating cancer registries. Eleven are National registries covering the entire populations. Sixty-five are regional and cover only a percentage of their country's population with coverage varying from 3% to 62% of the population.

The purpose of the EUROCARE project is to estimate and compare the cancer survival in European populations. The current EUROCARE database contains data on incidence and life status of cancer patients diagnosed from 1978-1994 with follow up data until the end of 1998. The EUROCARE-1 project reported on survival between 1978 and 1985, EUROCARE -2 project reported on cancer patients diagnosed between 1985 and 1989 and the current EUROCARE-3 project has published survival data for cancer patients diagnosed in 1990-1994. The publications from this project have highlighted the marked differences in incidence, mortality and survival of colorectal

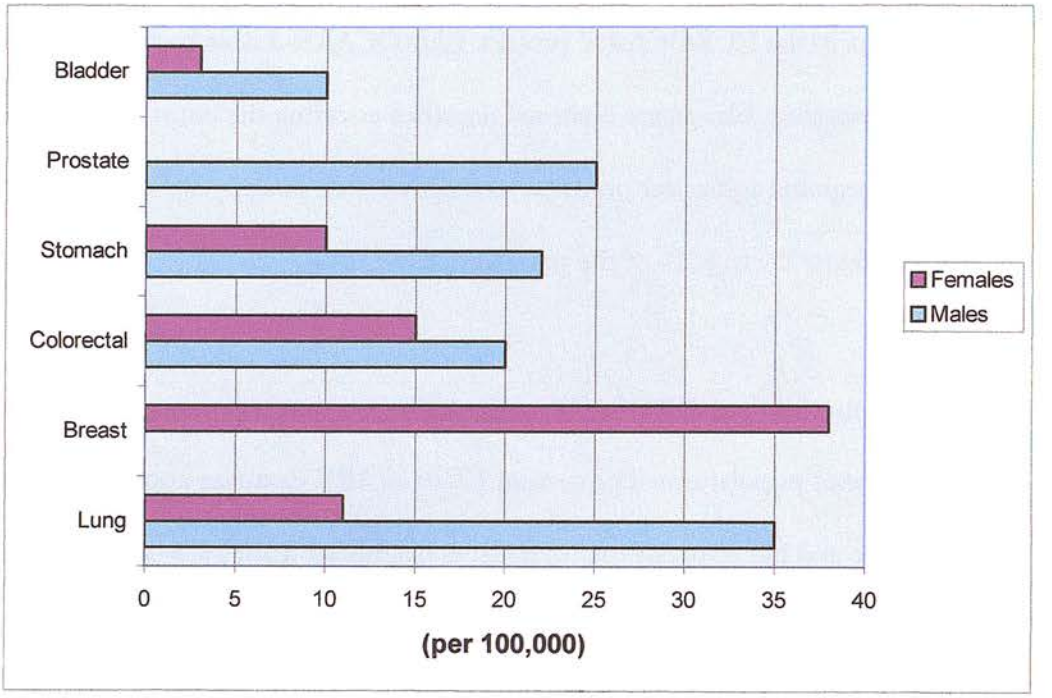
1 EUROCARE is a group of European epidemiologists and biostatisticians, funded by Biomed. They have collected data from 50 countries and 19 cancer registries from 1978-1995.

cancer in Europe. The EUROCARE project has been criticised for the differences in the data collection methods, the varied quality of data provided by the registries and the differing methodologies used in the analysis (Woodman et al 2001).

Worldwide Incidence

Internationally it is the fourth highest cause of cancer deaths in men and women. Figure 1 illustrates the worldwide number of cases and deaths from the more common cancers.

Figure 1 ***World number of cases with common cancers, by sex. Age standardised rate per 100,000 (all ages)***

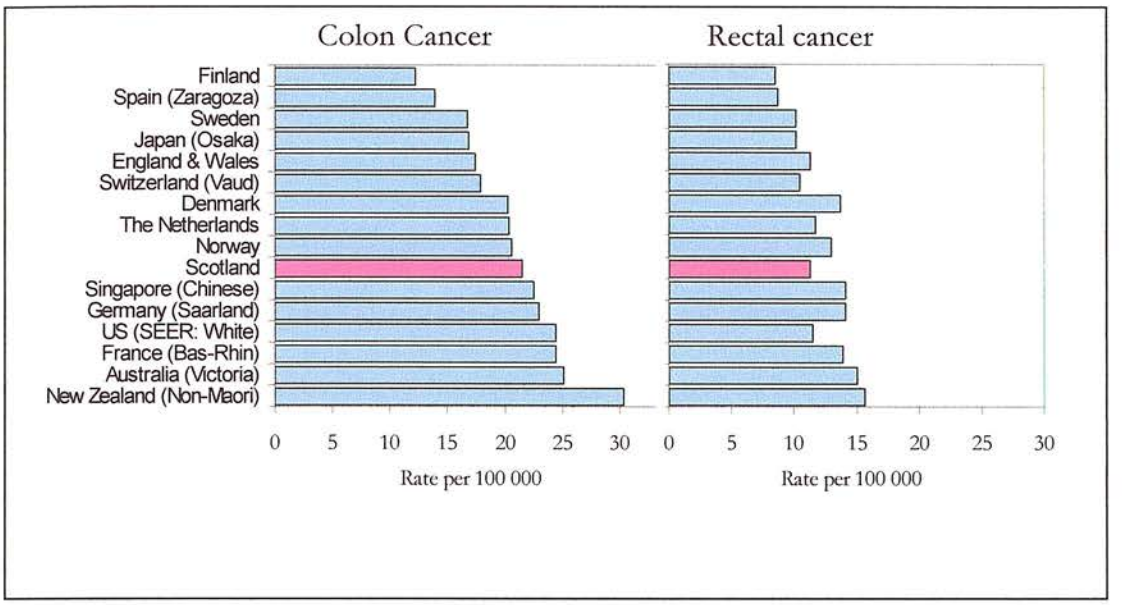


(Adapted from GLOBOCAN 2002, IRAC).

Colorectal cancer has the 4th highest incidence of common cancers in males and the 3rd highest incidence of common cancers in women. Figure 2 below, demonstrates that Scotland has a higher incidence for colon cancer than most other European countries. However, the incidence in Scotland is lower than in USA, Singapore, France, Germany,

Australia and New Zealand. Throughout the world there is a higher incidence of colon cancer than rectal cancer. The incidence of rectal cancer in Scotland is similar to most European countries and USA.

Figure 2 Comparison of International colorectal[2] cancer incidence, 1988-92[3]



Adapted from Cancer Incidence in Five Continents, Volume VII (1997)

Incidence in Europe

The EUROCARE project covers all cancers and information on colorectal cancer incidence, comparing Scotland with England and Wales and two Scandinavian countries can be seen in Table 1.

2 Defined here as ICD10 C18-C21

3 The Netherlands data includes the period 1989-92, England and Wales includes 1988-90, Spain includes 1986-90 and Finland includes 1987-92

Table 1 ***Incidence of colorectal cancer per 100, 000 based on cancer registration in 1995, (standardised to the world standard population), by sex***

	Males	Females
Scotland	**41.1**	**29.6**
Denmark	37.8	28.6
England and Wales	35.7	27.8
Finland	26.5	19.2
Sweden	29.4	22.9

(Gatta *et al* 1998)

Table 1 shows that Scotland has a higher incidence than comparable European countries. It is recognised that cross-country comparisons are flawed and the results can be difficult to interpret due to variation in data quality and variation in definition of malignancy. Therefore, bias may be introduced by sub national cancer registration (Berrino et al 2001).

Incidence in England and Wales

Colorectal cancer is the third most common cancer in males and second most common cancer in females in England and Wales. England and Wales incidence, mortality and survival data in this thesis are taken from the Office of National Statistics (ONS 2004).

England

In 1997, a diagnosis of colorectal cancer was made in 28,900 individuals; it occurs more frequently in males and incidence has continued to increase for both sexes. Within the colorectal figures 63% of cases were diagnosed as colon cancer and 37% as rectal cancer.

Between 1971 and 1997 the overall standardised incidence in males rose by 30% for colon cancer compared with an increase of 6% in rectal cancer over the same period.

The female colon cancer incidence is approximately twice that of rectal cancer in females (Quinn et al 2001).

Wales

In Wales, the incidence is published separately for colon and rectal cancer. The incidence is higher in males for both colon and rectal cancer. Colon cancer is the third most common cancer in both sexes. During 1992-2001 colon cancer was responsible for 8.4% of all male cancers and 8.5% of all female cancers. There were 640 males and 570 females diagnosed with colon cancer in 2001. In recent years, there has been a slight decrease in colon cancer incidence in females but not in males.

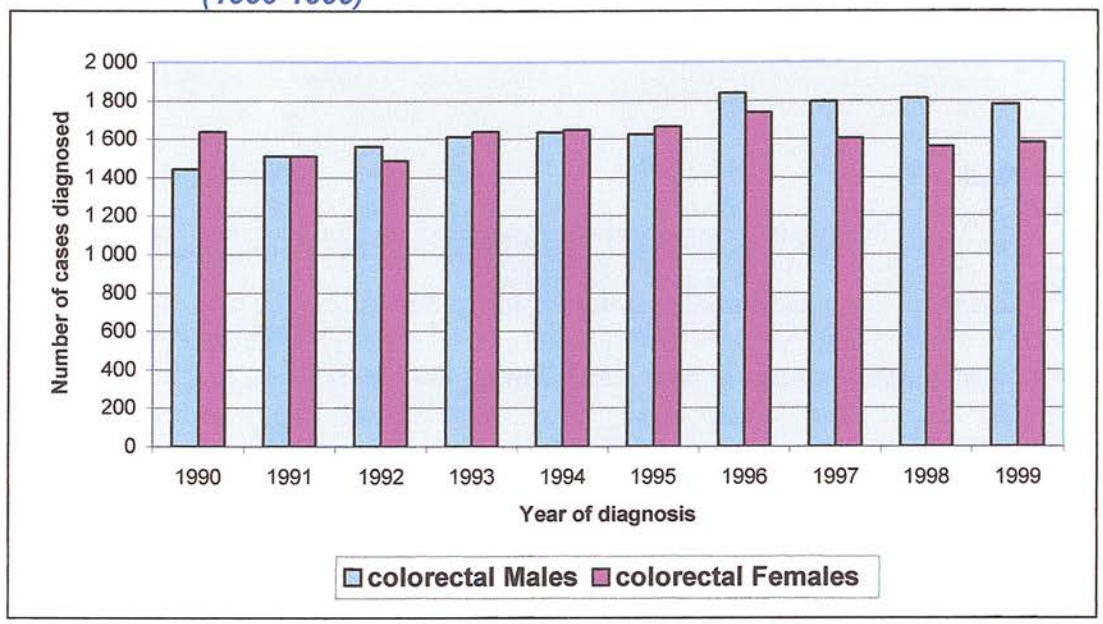
Rectal cancer was the fifth most common cancer in both sexes during 1992-2001 and was responsible for 6.1% of all male cancers and 4.1% of all female cancers. There were 440 males and 293 females in 2001 diagnosed with rectal cancer (Welsh cancer intelligence unit, 2003).

Incidence in Scotland

Colorectal cancer

In Scotland, colorectal cancer (cancer of colon and rectum together) is ranked as the third most frequent cancer diagnosed in both sexes. Of all cancers diagnosed in Scotland, colorectal cancer is responsible for 15.1% in males and 12.2% in females. There is a higher incidence of colorectal cancer in males. During 1990 to 1999 there has been a 22.8% increase in male incidence and only 2.4% increase in females. Figure 3 illustrates the number of males and females in Scotland for over this period.

Figure 3 ***Number diagnosed with colorectal cancer in Scotland (1990-1999)***



(Adapted from ISD 2003)

Forty five percent of patients with colorectal cancer are over 75 at diagnosis and the population is ageing. Therefore over the next decade, the incidence of colorectal cancer in Scotland is not expected to decreased .

Colon cancer

In Scotland, colon cancer is responsible for 9.2% of all cancers diagnosed in males and 8.7% in females. In 1999, 1,124 females and 1,083 males were diagnosed with colon cancer. Although females have a greater incidence of colon cancer, it has fallen by 2.8% in the decade 1990-99. In contrast, male incidence of colon cancer increased by 14.9%.

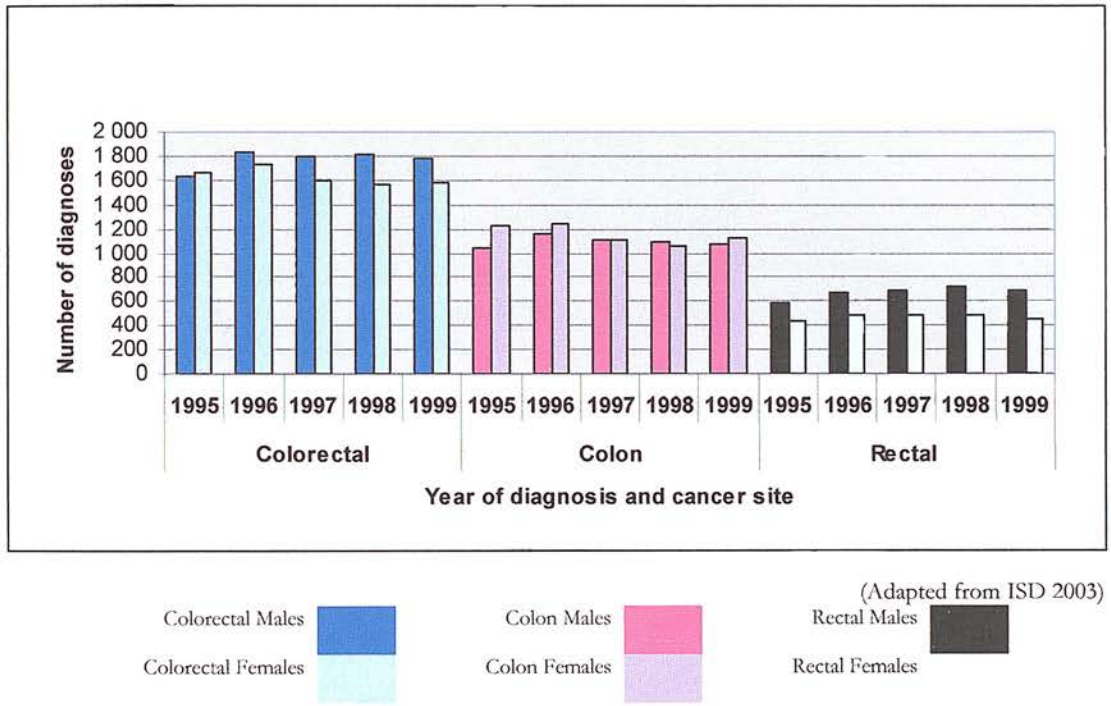
Rectal cancer

In Scotland, rectal cancer is responsible for 5.9% of all cancers diagnosed in males and only 3.5% in females.

Rectal cancer in males has a much higher incidence than in females and in 1999, 69% of cases were males. During 1995 to 1999, there has been an alarming increase in incidence of rectal cancer with an increase of 37.9% in males and of 17.1% in females.

When colorectal cancer is divided into colon and rectal a different sex pattern emerges. Females have a higher incidence of colon cancer, although this is changing slightly due to falling incidence in females and a rising incidence in males. In rectal cancer there is a wide gap between males and females. Figure 4 shows the incidence of colorectal cancer, colon cancer and rectal cancer 1995-1999.

Figure 4 ***Number of cases diagnosed with colorectal cancer, colon and rectal cancer in years 1995-99***



(Adapted from ISD 2003)

Colorectal Males
Colorectal Females
Colon Males
Colon Females
Rectal Males
Rectal Females

When a comparison of incidence in Scotland, England and Wales is made there are clear differences in incidence, as shown in table 2.

Table 2 Crude incidences per 100,000 for England[4] and Scotland[5] 1999 and Wales in 2000[1]

	Scotland		England		Wales	
Cancer site	Males	Females	Males	Females	Males	Females
Colon	43.6	42.7	35.9	35.8	45.1	39.8
Rectal	27.9	17.3	24.5	16.8	32	18.2

(ISD 2003, ONS 2004)

The highest male incidence of colon cancer is in Wales and highest female incidence in Scotland. Wales has the highest rectal cancer incidence for both sexes.

4 Data extracted from Office for National Statistics website (www.statistics.gov.uk)

5 Data extracted from Scottish Cancer Registry, Information and Statistics Division (www.show.scot.nhs.uk) ISD online

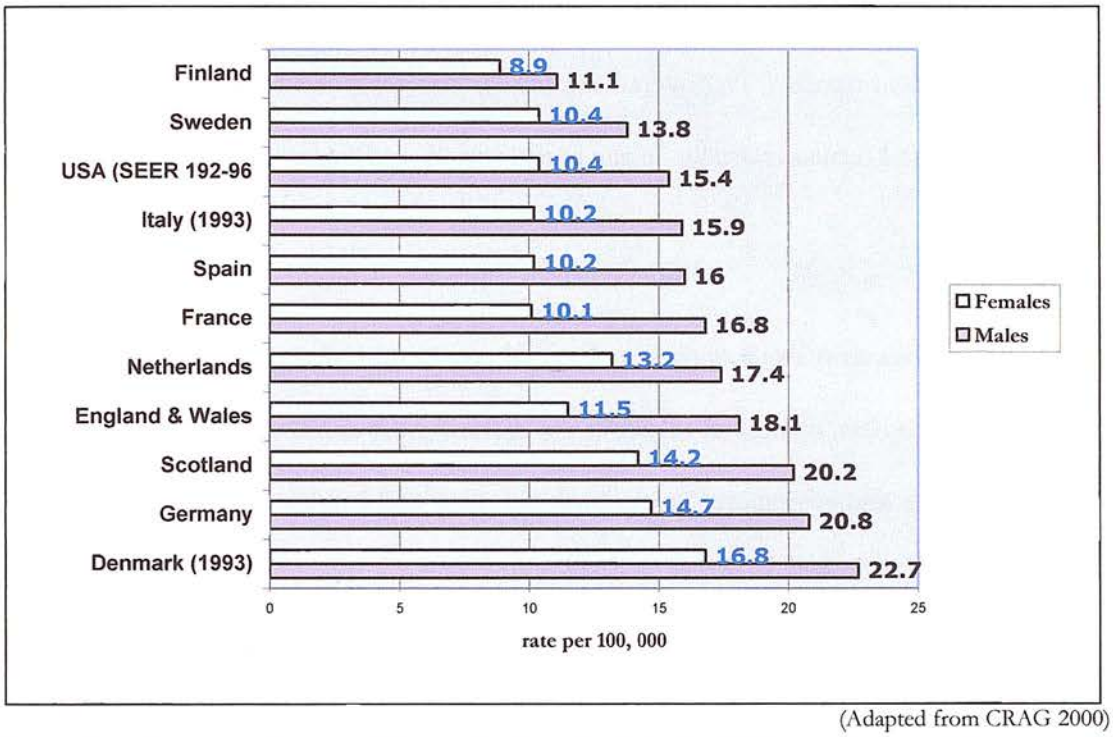
Chapter 3

Introduction to Mortality from Colorectal Cancer

Colorectal cancer mortality

In most European countries mortality from colorectal cancer had been decreasing over recent years. Figure 5 indicates the colorectal cancer international mortality rates in 1995 by sex.

Figure 5 *Colorectal cancer: International comparisons of mortality rates (world standard population), by sex: 1995*



(Adapted from CRAG 2000)

International comparison rates show that Scotland had a similar mortality rate to England, Wales, Germany and Denmark, but much greater mortality than the USA where the incidence is greater than most European countries.

England and Wales

In the year 2002, colorectal cancer was responsible for 10% of all cancer deaths in the UK, second only to lung cancer. It is responsible for 11% of all cancers in men and 10% of all cancers in women.

England

When compared to all common cancers in the year 2002, colorectal cancer had the third highest mortality rate for males and fourth highest for females. Colorectal cancer mortality in both sexes has fallen steadily since the 1950s. Colon cancer mortality has declined by 53% in females during this period to reach a level of 12 per 100,000 in 1999. In the 1950s, colon cancer mortality in males was 24 per 100,000; this had dropped to 16 per 100,000 by 1999. The decrease in mortality for males is less than for females. By 1999, rectal cancer mortality had fallen by 56% to 9 per 100,000 in males and to 5 per 100,000 in females. The overall decrease in mortality masks a slight rise in male colorectal cancer mortality in the age group 85 and over.

Wales

Wales has seen a reduction in colorectal cancer mortality rate for both sexes. However, of all cancers, colorectal cancer is the second most common cause of cancer death in Wales, a higher ranking than in both Scotland and England.

Scotland

In Scotland, colorectal cancer has shown a minimal decrease in mortality rate. The crude mortality rate reported for colorectal cancer in 1992 was 34.6 per 100,000 and was 34.3 per 100,000 in 2001. Mortality rate decreased between 1960 and 1999 except for male rectal cancer, which after an initial fall, continued to rise to levels previously seen in the early 1960s (Gray et al 2002). The largest fall in colorectal cancer mortality rate is seen within the first year after diagnosis.

Scotland has a higher mortality rate than England and Wales in both sexes for rectal cancer and mortality rates are only marginally better than Wales for female colon cancer. These higher mortality figures in Scotland reflect the high incidence and the lower survival rates. Table 3 compares the crude colon and rectal cancer mortality rate per 100, 000 for males and females in year 2000 for Scotland, England and Wales.

Table 3 ***Colon and rectal cancer crude mortality rates, per 100,000 for England, Scotland and Wales in 2000***

Cancer site	Scotland		England		Wales	
	Male	Female	Male	Female	Male	Female
Colon	21.2	20.4	19.5	18.7	26.2	21.8
Rectal	13.3	8.4	10.5	7.5	10.7	7.7

(ISD 2003 and ONS 2004)

Despite decreasing mortality rates in the UK, there still remain differences between England, Wales and Scotland. Wales had over 6% higher mortality rate than England and 5% higher than Scotland for male colon cancer. Scotland has a 3% higher mortality in male rectal cancer than England and Wales.

Chapter 4

Introduction to Survival from Colorectal Cancer

Colorectal cancer survival

Population based survival estimates are a key indicator of the overall effectiveness of healthcare systems in managing cancer patients. Stage of disease at diagnosis is an important factor in survival (Mulcahy & O'Donaghue 1997, England et al 1998); therefore, every country is striving to diagnose colorectal cancer at an early stage to improve survival rates.

International and European survival

The Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute is an authoritative source of information on cancer incidence and survival in the United States. The SEER Program currently collects and publishes cancer incidence and survival data from 14 population-based cancer registries and three supplemental registries, covering approximately 26 percent of the USA population. The SEER registries routinely collect data on; patient demographics, primary tumour site, morphology, stage at diagnosis, first course of treatment, and follow-up for vital status. Survival rates show marked differences between SEER and EUROCARE projects, for most cancers and in particular in the older age group.

In colorectal cancer the survival gap by age was not as great as seen in other cancers that have a higher prevalence in the older age group. This implies that lower survival in Europe cannot be explained by age related biological factors, such as comorbidity, immune function and responsiveness to drugs (Coleman et al 2003). The greatest survival rate for colorectal cancer is seen in the first six months after treatment;

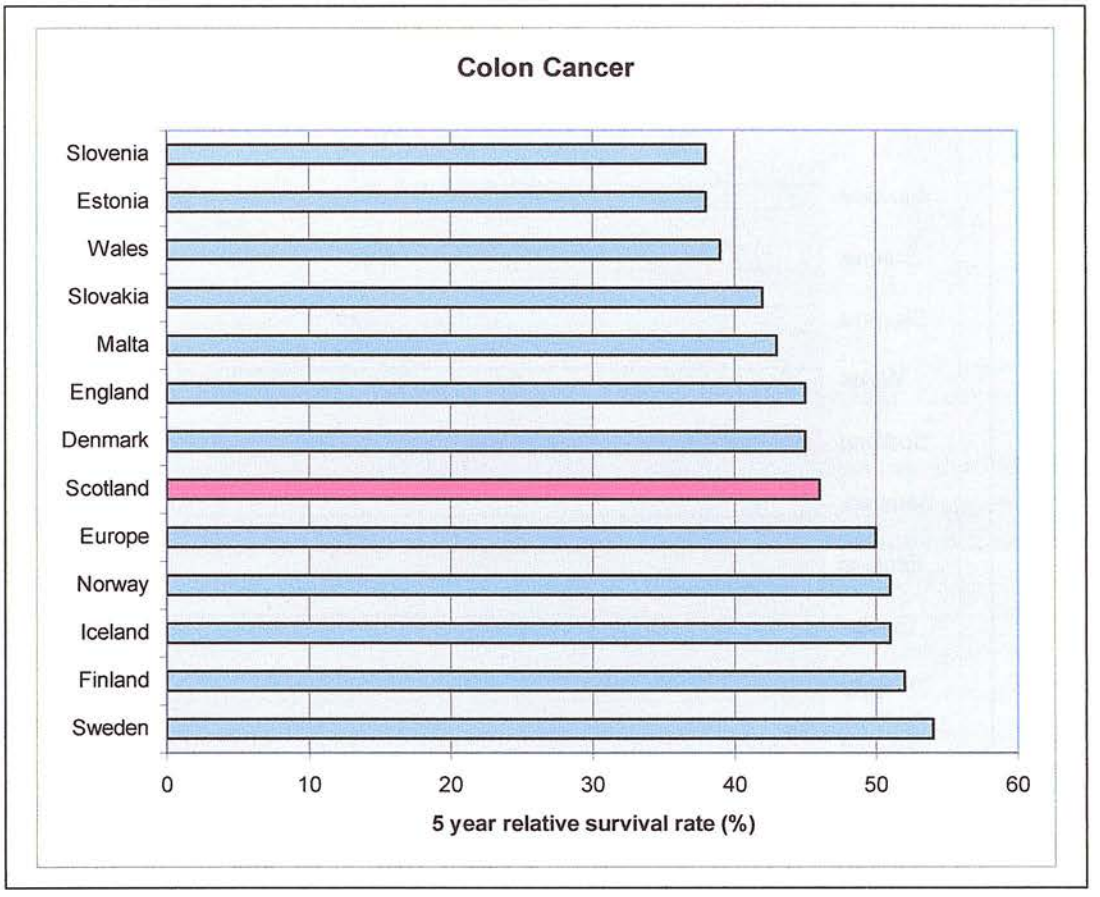
suggesting that there are effects from stage at diagnosis and/or access to optimal care (Sant et al 1995, Gatta et al 2000).

Survival in adult cancer falls with age even after adjustment for mortality from other causes. Although not so marked in colorectal cancer, there is an age survival difference. The five-year relative survival rate of the group aged 15-44 is 59% compared to those aged 75 and over who have only 42% survival rate.

Colorectal cancer five-year relative survival rate for males diagnosed in 1990-94 in the EUROCARE-3 project, have a much wider range than the areas covered in the SEER dataset within USA. The highest survival rate in EUROCARE–3 did not reach the lowest survival rate in SEER. The EUROCARE-3 range is 27-55% and SEER range is 60-65% (Coleman et al 2003). It should be noted that SEER do not publish age standardized survival rates.

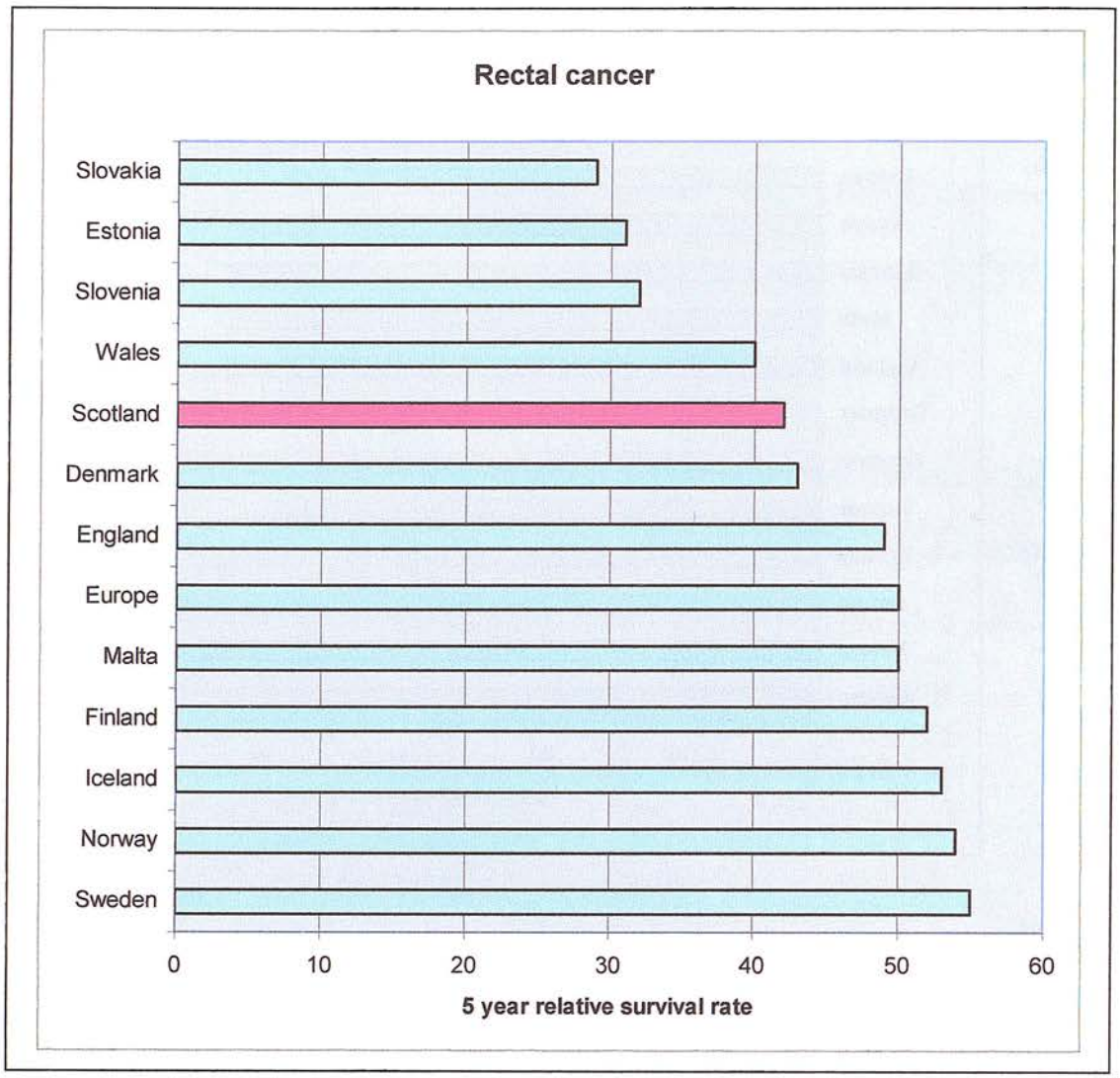
Figures 6 and 7 show the five-year relative survival rates of colon and rectal cancer for people from European countries where the cancer registry coverage is 100%, with the exception of England where the coverage is 63%. These figures are compared to the overall European five-year survival rate.

Figure 6 ***Five-year relative survival rates (%) of colon cancer for those diagnosed 1990-1994 (European age standardised)***



(Adapted from Sant et al 2003)

Figure 7 ***Five-year relative survival rates (%) of rectal cancer for those diagnosed 1990-1994 (European age standardised)***



(Adapted from Sant et al 2003)

England and Wales

Survival in England and Wales from colon and rectal cancer has improved over time but only a small impact on five-year relative survival rate was achieved. Table 4 demonstrates the increase in survival over two five-year periods.

Table 4 ***Five-year relative survival rate by site of colorectal cancer and by sex for England and Wales combined.***

Site		Five year survival rate	
		1991 - 1995	1996 – 1999
Colon	Male	42%	47%
	Female	43%	48%
Rectal	Male	40%	47%
	Female	45%	51%

(Rowan & Brewster 2004)

Survival from colorectal cancer has shown a smaller age difference than many other cancers. Five-year relative survival in 1999 from colon cancer in those aged 40-79 was approximately 50% and for those age 80-99 approximately 35% with little difference between the sexes in all age groups (Quinn et al 2001).

Scotland

Despite continued improvement in survival rates in Scotland, three in five colorectal cancer patients die as a direct result of their cancer within five-years of diagnosis. Survival rates have been improving since 1971; however, survival rate decreases with increasing age in both sexes. Survival rate is more favourable in young females.

Survival at one-year for colon cancer in 1971 was 44% and increased to 66% by 1997. Five-year survival in 1971 was 28% and increased to 45% in 1997. Rectal cancer one-year survival in 1971 was 54% and increased to 71% in 1997. The five-year survival in 1971 was 28% and increased to 44% in 1997. Six years after diagnosis, colon cancer patients revert to the population survival risk. However, rectal cancer patients continue to die from this cancer for more than 10 years after diagnosis. These figures have

continued to improve as shown in table 5. Females have better survival rates in all sites with the greatest advantage seen in rectal cancer.

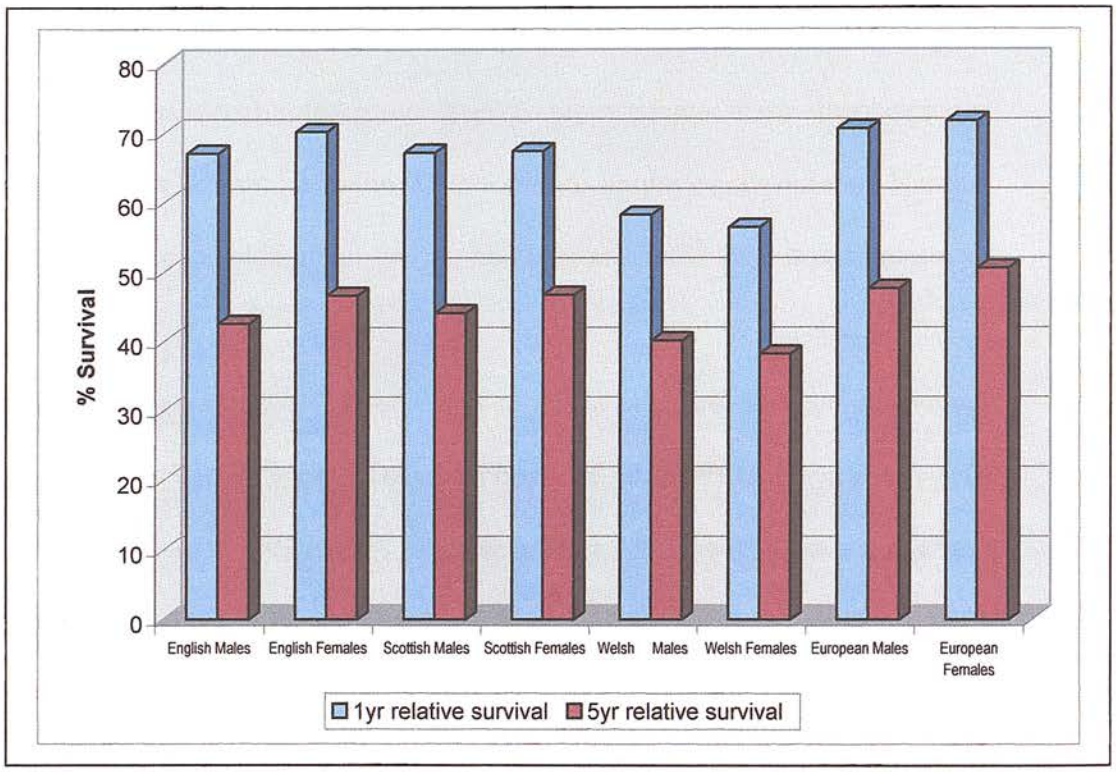
Table 5 One-year and five-year relative survival rates in Scotland

Cancer site	One year survival		Five year survival	
	Males	Females	Males	Females
Colorectal Diagnosed **1991-95**	67.7	65.5	44.1	45.1
Colon Diagnosed **1996-98**	70.7	67.2	48.8	48.9
Rectal Diagnosed **1996-98**	74.8	76.7	48.3	51.9

(ISD 2003)

In 1997, one-year survival in females with rectal cancer was marginally higher that males with rectal cancer. Figure 8 illustrates the one and five-year relative survival rates in England, Wales and Scotland, Europe.

Figure 8 One-year and five-year relative survival rates in England, Wales, Scotland and Europe, for those diagnosed in 1991



(Adapted from IRAC 2000)

Figure 8 demonstrates that England, Wales and Scotland have poorer one and five-year survival rates than Europe. Although survival rates are increasing in Scotland, England

and Wales they still remain below survival rates in many other European countries, which in turn, have much lower survival rates than the USA.

Survival and tumour staging

Colorectal cancer is given a stage to represent the extent of the disease and as an indicator of prognosis. There is an internationally recognised classification known as Dukes' staging. Sir C.E. Dukes, a British pathologist, created this in 1929 for rectal cancer. Simpson and Mayo modified Dukes' scheme for colon cancer in 1939. This system graded the tumours at three different stages, Dukes' A, B and C. Astler and Coller in 1967, made further modifications to include stage D, for distant metastasis and inoperable cancers. The Dukes' staging system and its modifications are still in use by many clinicians. In 1998, the Tumour, Node and Metastasis (TNM) system was modified to correspond with the Dukes' system. More recently, the American Joint Committee on Cancer updated the TMN staging system. A summary of the Dukes' and the TNM staging systems, used in Scottish pathology laboratories can be seen in *(Appendix 6).*

Dukes' stage and survival

Dukes' stage is one of the most powerful predictors of survival from colorectal cancer. Five-year relative survival with a tumour staged Dukes' A is 85%, Dukes' B is 65%, Dukes' C is 40% and Dukes' D is <5% (Mulcahy & O'Donoghue 1997). Therefore, earlier diagnosis of colorectal cancer should reduce mortality and increase survival rates. However, this may be difficult to achieve. The nature of colorectal cancer is such that some tumours may not present with symptoms until at an advanced Dukes' stage (Dent et al 1983). Few publications compare Dukes' stage of tumour between countries, as this

is not normally collected in cancer registries. The EUROCARE project is addressing this with the development of high-resolution studies, which have requested incorporation of Dukes' stage into all cancer registries.

Distribution of Dukes' stage in Europe

Gatta et al (2000) published data from a EUROCARE high-resolution study; this study comprises of a selection of 11 registries that were asked to supply a representative sample of at least 200 consecutive colorectal cancer patients from those diagnosed in 1990 or over the period 1989 to 1991. The results of this study were presented with the Dukes' staging A and B combined into one group.

Table 6 illustrates the highest and lowest percentages for each Dukes' stage of tumour found at diagnosis in European countries that are involved in the EUROCARE project.

Table 6 Dukes' stage (%) at diagnosis from EUROCARE high-resolution study on colorectal cancer

Dukes' stage	Distribution of Stage at diagnosis (%)	
	Highest	Lowest
A & B	58% Rotterdam, The Netherlands	21% Cracow, Poland
C	25% Cote d'Or, France	18% Cracow, Poland
D	27% Varese, Italy	14% Cote d'Or, France

(Gatta et al, 2000)

These figures illustrate the marked differences between European countries. There are numerous differences between the cancer registry populations making comparisons difficult to interpret (Woodman et al 2001). Gatta et al (2001) have published the 3-year observed survival rate relative to Dukes' staging. It demonstrates the decline in survival

with more advanced Dukes' staging at diagnosis. Table 7 shows the large differences between countries in the initial staging of individuals at presentation.

Table 7 Three-year survival (%) by Dukes' stage at diagnosis from EUROCARE high-resolution study on colorectal cancer

Dukes' stage	Three year survival (%)	
	Highest surviving	Lowest surviving
A & B	85% Calvados, France	56% Cracow, Poland
C	55% Cote d'Or, France	28% Varese, Italy
D	25% Modena, Italy	6% Mersey(UK) & Cote d'Or

(Gatta et al 2000)

England

Currently the distribution of Dukes' staging is not routinely published for England and Wales. The NHS has commissioned the development of a data set for all cancer patients in which Dukes' stage is included (www.nhsia.nhs.uk).

The EUROCARE high-resolution study has shown little difference in the distribution of Dukes' staging in two areas of England. However, within these two areas there was a difference in the 3 year observed survival rates with specific reference to the unknown category, as seen in table 8.

Table 8 Three-year survival in Mersey and Thames by Dukes' stage

Dukes' stage	Distribution of Dukes' stage		Three years survival (%)	
	Mersey	Thames	Mersey	Thames
A & B	40	42	78	61
C	23	24	48	30
D	23	23	6	10
Unknown	14	11	23	32

(Gatta et al 2000)

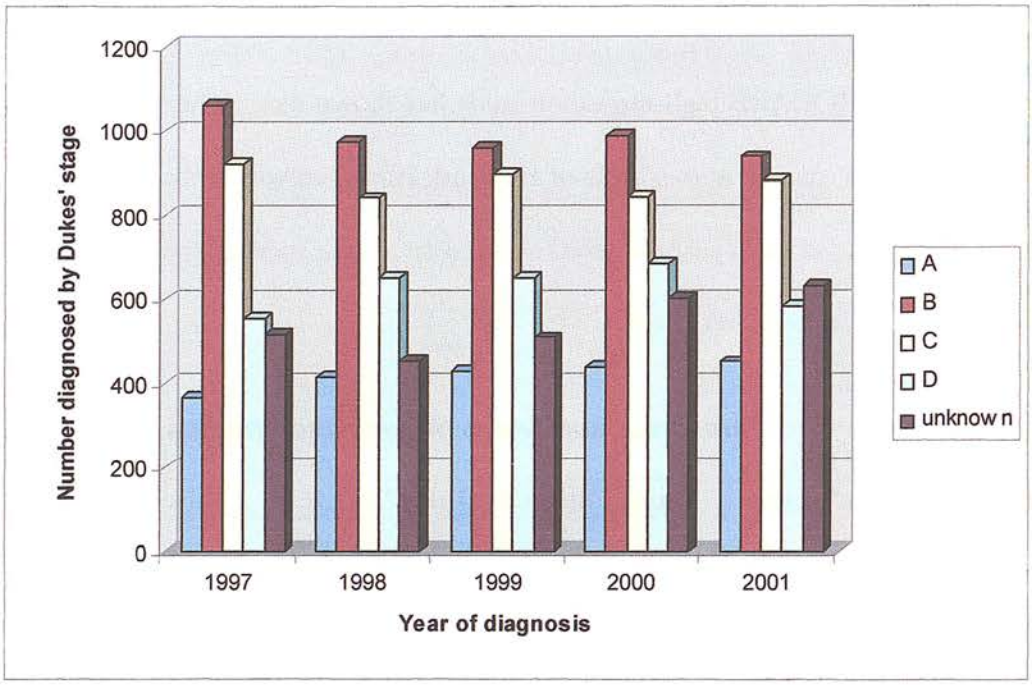
Mersey had a higher survival rate for Dukes' stages A & B and C. Thames demonstrated an increased survival rate for those who did not have a staging. It is possible that

Thames has a high number of polyp cancers, which were not staged leading to an increased survival in this group and Mersey may have included these polyp cancers in their Dukes' stage A cancers.

Scotland

The Scottish Cancer Registry database includes Dukes' staging data and information was requested specifically for this thesis from the Information Services Division of the Scottish Cancer Registry. Data in this thesis may differ from other Dukes' stage published figures because the dataset is dynamic and changes as new information is received at the registry. Figure 9 indicates the colorectal cancer Dukes' stage distribution by year of diagnosis over a five-year period. (www.isdscotland.org)

Figure 9 Dukes' stage distribution in Scotland (1997-2001)



(Adapted from ISD 2003)

It can be seen from Figure 9 that over the period 1997-2001 there was a slight increase in Dukes' stage A, a decrease in Dukes' stage B, little change in Dukes' stage C and an slight decrease from 1998 for Dukes' stage D.

There are a significant number of cancers with an unknown Dukes' stage. The numbers in the unknown stage category have increased over the years. Each year the numbers in the stage unknown group was higher than the number of Dukes' A tumours. The number with Dukes' A tumours in 2001, was 450 and the number with unknown staging was 601. The increased number of unknown cancers may indicate that more polyp cancers have been identified. This is feasible since the Faecal Occult Blood Testing (FOBT) pilot was introduced in the year 2000 in the Tayside, Fife and Grampian areas of Scotland. In the year 2000 the number of unknown staged cancers was 508 and this increased to 601 in 2001 and 632 in 2002.

Summary of incidence, mortality and survival

The incidence of colorectal cancer is increasing worldwide. Scotland has a lower incidence than United States of America as published by the SEER project, Australia, Germany and France. In the United Kingdom, Wales has the highest incidence of colorectal cancer in both sexes. Recent figures have shown been a decrease in incidence in Wales however they remian the highest incidence figures in the UK. In England, colon cancer incidence has increased more than rectal cancer. In Scotland, the incidence of rectal cancer is greater in males and the incidence of colon cancer is greater in females.

In the United Kingdom, Wales has the highest mortality rate for colon cancer. Scotland has the highest mortality rate for rectal cancer. Throughout the UK mortality has fallen steadily in both sexes. England and Wales have shown a greater reduction in mortality in rectal cancer. Survival from colorectal cancer is increasing worldwide but there remain

large differences between European countries and SEER. In the United Kingdom, Wales has the poorest survival rates from colorectal cancer.

The above data from the EUROCARE project include anal cancer and anal canal cancers, whereas the Scottish Registry data do not include anal cancers.

Although there is a plethroa of statistics available from European and US databases on incidence, mortality and survival of colorectal cancer some caution should be exercised interpreting the results from cross country analysis for the reasons given below:

- Data collectors Have difficulty in maintaining the quality of the data sent from each country.
- The percentage of populations covered by each cancer registry varies between and within countries.
- Some cancer regirsties have more robust systems of collecting cancer registry data from the sources of diagnosis that other countries.
- Ethincicty and cultural issues are also likely to have a role in some aspects cancer diagnosis.

Chapter 5

Family History of Colorectal Cancer

Inherited susceptibility to cancer

Introduction

In the last twenty years the developments in molecular genetics and database technology, have lead to greater understanding of inherited cancers and the implications for affected individuals and their families. This new understanding led to the identification and collection of large families with many cancers. Linkage analysis was possible in some families which lead to identification of cancer susceptibility genes and definition of cancer specific penetrance. These findings drove the development of criteria to identify families that would give the scientists the highest chance of finding other genes responsible for increasing risk of common cancers. When the first highly penetrant multi-factorial genes for breast cancer were cloned the clinical genetic departments responded to the demand for a service which offered family history risk assessment, screening recommendations, genetic testing for high-risk individuals and DNA storage for those not wishing testing or moderate risk family history.

Genetics of colorectal cancer

Familial Adenomatous Polyposis (FAP)

Familial Adenomatous Polyposis (FAP) was first described over 100 years ago and was recognised as having an autosomal dominant inheritance pattern. The gene responsible for FAP was identified in 1991 (Kinzler et al 1991) and is known as the APC gene. FAP cases are responsible for approximately 1% of all colorectal cancers.

Mutations in the APC gene are strongly associated with both inherited and sporadic cases of colon cancer. The APC protein, like many tumour suppressors genes, functions

controls the expression of genes critical in the cell division process. Inactivation of the APC gene, located on chromosome 5, is thought to lead to increased cell proliferation and contribute to the formation of colonic polyps. Several genetic alterations must occur during the conversion of normal colon cells into cells capable of forming tumours. Mutation of the APC gene is thought to be one of the early steps in the process of tumourigenisis.

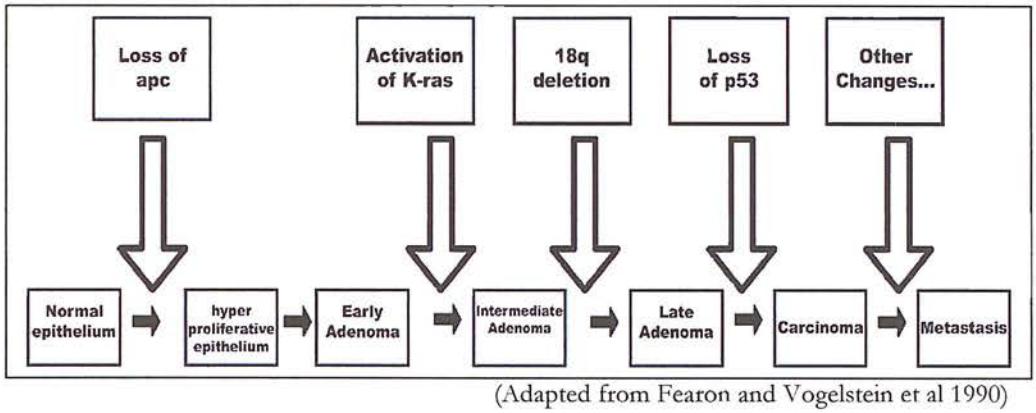
FAP is characterised by early onset colorectal cancer with hundreds to thousands of polyps. Every polyp has the potential to develop into a cancer therefore those with the inherited mutation are at a much higher risk of developing colorectal cancer. This situation is very similar to the one described for the inherited form of retinoblastoma.

Following the identification of the APC gene, family studies identified that de novo mutations in the APC gene are responsible for approximately 25% of all new cases. There are also many extra-colonic cancers observed in cases of FAP such as; desmoid tumours, multiple craniofacial and long bone osteomata, epidermoid cysts and retinal pigmentation.

Although the APC gene is known to cause FAP through germline transmission, mutations of the APC gene are also found in over 80% of sporadic colorectal cancers. This finding led to a model that proposed that multiple events were required for tumorigenesis to complete. This model developed by comparing the mutations identified in cells removed at different stages of cancer development, a possible order for genetic mutations that led to a subset of colon cancers. In this model, the APC gene is mutated in the first step, producing highly proliferative cells. Those cells will then

form a polyp, which may develop into cancer. Figure 10 demonstrates the multistep process of cancer.

Figure 10 Multistep process of cancer



(Adapted from Fearon and Vogelstein et al 1990)

Although presented as a linear diagram, it is now thought that these events do not need to follow a linear time-frame.

Colorectal cancer, like other cancers, results from the exposure of normal cells to a series of toxic events that result in the accumulation of mutations in key genes that force the cells into proliferation. It is thought that approximately three to six different mutations are required for the transformation of a normal cell into a cancer cell.

As colorectal cancer is more prevalent in the older age group, this is consistent with the above theory of multiple accumulations of errors, which includes inactivation of tumour suppressor genes and mutation activation of oncogenes for the cell to become a cancer cell. Having one mutated gene increases the chance of more mutations in the same cell due to impairment in DNA repair. It is most likely that additional interactive effects

between genetic and environmental factors also play a role in cancer development (Dicato et al 2000).

Each mutation reduces the timescale for a cell to transform from a normal cell to a cancer cell and the mutation significantly increases the risk, in these individuals, of developing a cancer and at a much younger age, than normally seen in the general population.

Family history

Family history is a known risk factor for colorectal cancer, especially in families with Familial Adenomatous Polyposis (FAP) or Hereditary Non Polyposis Colorectal Cancer (HNPCC) mutations. Although these mutations are relatively rare, individuals with a known gene mutation are at a very high risk of developing colorectal cancer.

More recently, it has been accepted that a families whose history of colorectal cancer does not meet the recognised high risk Amsterdam criteria also have increased risk of colorectal cancer, compared to the general population. Various studies have shown that first degree relatives of individuals with colorectal cancer are at a 2 to 3 fold increased risk of developing colorectal cancer (St John et al 1993, Slattery et al 1994, Johns et al 2001). This has led to the production of risk and surveillance criteria for those with a moderately increased family history risk.

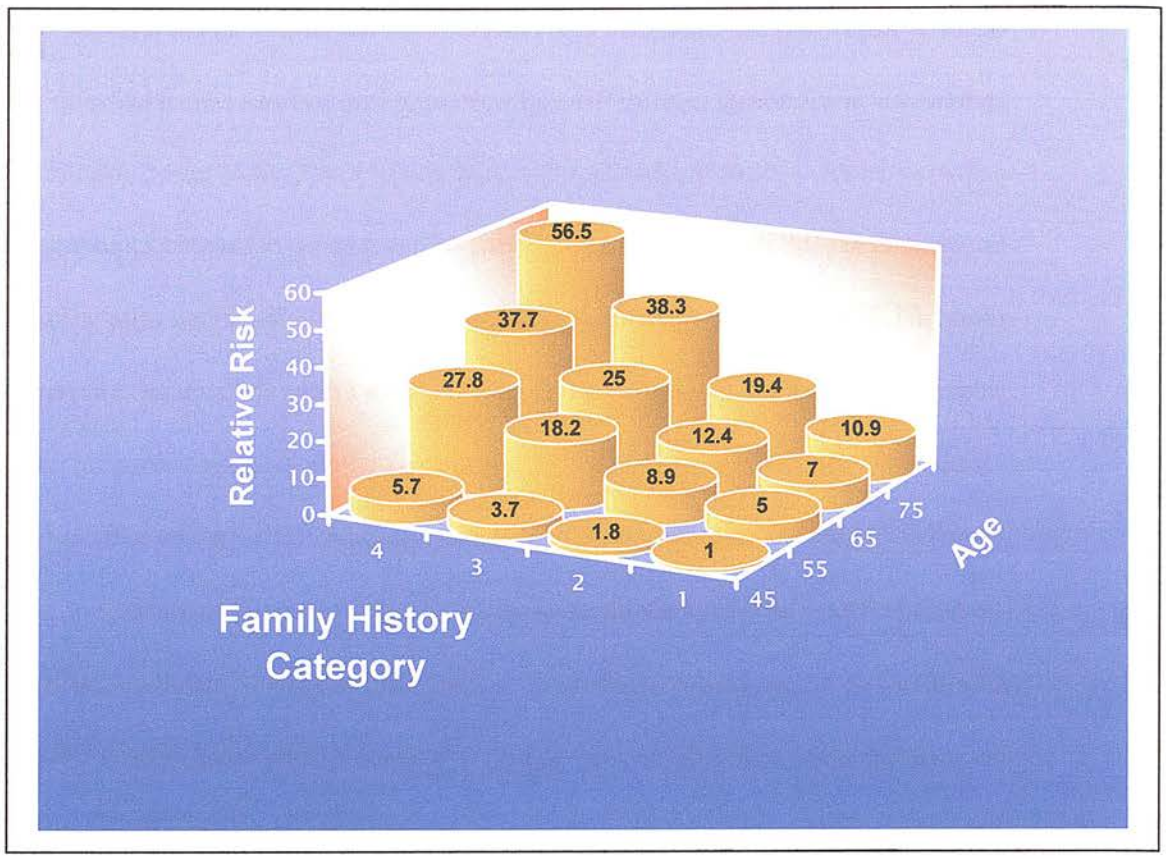
It is estimated that within the general population no more than 7% have an affected first-degree relative with colorectal cancer (House et al 1999, Sadhu et al 2002, Wallace et al 2004). Despite this small percentage within the population meeting the criteria of one first-degree relative with colorectal cancer, if screening was implemented at this risk

a large number of individuals would require colonoscopy surveillance. It has therefore become important for moderate risk criteria to be developed to ensure that those individuals at increased risk are offered screening but without overwhelming the NHS.

St Johns et al (1993) published data on risk of developing colorectal cancer as an odds ratio of 1.72 for any family history of colorectal cancer, 3.7 for one affected relative under age 45 and 5.7 for two affected relatives with colorectal cancer. Alternatively Houlston et al (1990) reported risk as lifetime risk of developing colorectal cancer and found 1:17 with any family history of colorectal cancer, 1:10 with an affected relative under age 45 and 1:6 for two affected relatives with colorectal cancer.

The data can be confusing when used to relate risk to individuals in a clinical setting. A diagram of relative risk has been assembled produced from combining the data from St John et al (1993) and Johns & Houlston (2001) seen in Figure 11. This diagram is simple to interpret however risk expressed as relative risk is not well suited to clinical use. Risk of developing cancer in a particular time frame is more useful. Using one affected relative under age 45 and two affected relatives with colorectal cancer as the criteria the risk of developing colorectal cancer at the following ages is; 40 is 0.99%, 50 is 1.15%, 60 is 2.78% and at age 70 is 5.00% (Scottish cancer sub group 2001).

Figure 11 *Risk of colorectal cancer by age and family history*



Family History Category

1. No Family History
2. One affected first-degree relative, over 45 at diagnosis
3. One affected first-degree relative, under 45 at diagnosis
4. Two affected first-degree relatives

(Permission to reproduce from Effective Health Care 2004)

General Practitioner and Family history

It has been suggested that GPs should have a 'gate-keeping' role to cancer genetic services (Campbell et al 1995). GPs should have the ability to identify and refer patients at increased risk to cancer genetic services and reassure those at low risk, as GPs are strategically placed and have the potential to care for several generations of one family at the same time (Harper et al 1996). However, GPs must have the knowledge and the willingness to undertake this role for this model to succeed.

In a randomised survey of physicians in the US, 95% self reported they take a family history as part of routine care (Hayflick et al 1998). Summerton and Garrod (1997) from

a postal questionnaire found that 29% of GPs stated they often/very often ask about family history. In a direct observational study within primary care where physicians were blinded to the reason for the study, Acheson et al (2000) observed that only 51% of new patients and 22% of established patients had family history discussed. Also, family history was less likely to be discussed if the patient was over age 65. This older age group are reported as an excellent resource of knowledge on several generations in a family. (Bannerman et al 1986, Aitken et al 1995).

Fry et al (1999) sought GPs views on their role in cancer genetic services and found that 60% of GPs were willing to take a detailed family history and make a referral to the regional cancer genetic services but did not feel they had the skills to assess risk or offer counselling based on the risk assessment.

Risk assessment and family history.

Cancer genetic clinics offer risk assessment and counselling with the options of genetic testing and/or surveillance when applicable. The testing and surveillance is offered as stated by local guidelines and surveillance availability in that area. These clinics also play a crucial role in identifying families eligible for research studies. However, the increased demand for this service has identified the necessity for referral to the clinic to meet high and moderate risk criteria of published guidelines to utilise the current cancer genetic services to the best advantage.

A recent study looking at the services provided by cancer genetic services in UK reported:

- An increase in referral rates,

- Inadequate numbers of cancer genetic staff,
- Inequalities in cancer surveillance and genetic testing offered (Wonderling et al 2001).

Wonderling et al (2001) explored the site distribution of cancer family history referred to 22 UK cancer genetic centres. This study reported that 61% of patients were referred because of concerns regarding breast cancer family history and only 16% for colorectal cancer family history concern. Individuals referred to the cancer genetic service with a risk not assessed as meeting the moderate or high-risk criteria for that region varied from 0% to 58% for all centres and in Scotland this figure varied from 26% to 33% (

Presently, genetic departments have low staffing levels and the considerable increase in referrals of individuals with a family history of cancer, particularly those not meeting moderate or high risk criteria, will increase the waiting times for all genetic patients. In Scotland, family history criteria and guidelines have been developed to address this issue.

Scottish family history guideline development

The Scottish Cancer subgroup on cancer genetics was formed by the Scottish Executive in response to the increasing demands on genetic services, for the provision of a cancer genetic service for individuals with a family history of cancer. This group approved a model of Genetic Associate[6] led cancer clinics previously piloted and evaluated in South East Scotland. The group also developed risk criteria and surveillance guidelines for use in the Genetic Associate led clinics and to assist other health professionals to determine when an individual has a relevant family history of cancer for referral to the cancer

6 Genetic Associate – refers to a Genetic Nurse Specialist or an individual completing a Masters Degree in genetic counselling.

genetic services. Within these guidelines the sub group defined three levels of risk that can be assigned to a family history.

The Scottish Executive published these risk criteria and surveillance guidelines and risk levels in March 2001 within a document 'Cancer Genetic Services in Scotland: guidance to the implementation of genetic services for breast, ovarian and colorectal predisposition'. These guidelines were also published within the Scottish Intercollegiate Guidelines Network (SIGN) guidelines for the management of colorectal cancer in March 2003. Both are freely available on (www.show.scot.nhs.uk) and (www.sign.ac.uk)

The following definitions are the three levels of risk:

High risk:

- At least 3 family members affected by colorectal cancer or at least 2 with colorectal cancer and one with endometrial cancer in at least 2 generations; one affected relative must be age <or=50 at diagnosis, one of the relatives must be a first degree relative of the other two
- HNPCC gene carriers
- Untested first degree relatives of known gene carriers

Moderate risk:

- first degree relative affected by colorectal cancer when aged <45 yrs;
- affected first degree relatives with 1 less than age 55 at diagnosis
- (one less than 55 years) or 3 affected relatives with colorectal cancer or endometrial cancer who are first-degree relatives of each other and 1 first-degree relative of the Consultand.

Low risk:

- Anyone not fulfilling high or moderate risk.

Table 9 lists the surveillance recommendations for those with a high and moderate risk family history as specified by the Scottish guidelines.

Table 9 Scottish Executive recommended surveillance guidelines

Surveillance recommendations for high risk
Two yearly colonoscopy from age 30 or 5 years younger than the youngest affected until age 70
Gynaecological surveillance for ovarian and endometrial cancer from age 35 years (research-based)[7]
Two yearly upper GI endoscopy (from age 50 or 5 years younger than youngest onset of stomach cancer)
Consideration needs to be given to surveillance for other cancers which may occur in specific families that are part of the HNPCC spectrum
Surveillance recommendations for moderate risk
A single colonoscopy at age 30-35, if findings are normal repeat at age 55. If normal no further surveillance
Incomplete colonoscopy should be followed by a barium enema preferably at the same hospital attendance.

(Scottish Cancer Genetic Sub Group 2001)

Colonoscopy surveillance of individuals with high or moderate family history risk has been shown to reduce morbidity and mortality (Vasen et al 1998, Jarvinen et al 2000). In order to implement these guidelines the cancer genetic sub group in Scotland proposed a two-tier cancer genetic service. The service suggested was:

- Primary care, oncologists and surgeons have a role to identify those at high and moderate increased risk and refer to cancer genetic services.

7 Ovarian surveillance is offered via a National research project

- Cancer genetic services would provide risk assessment, referral for surveillance and genetic counselling for testing, if appropriate.

This model relied heavily on the GPs, surgeons and oncologists identifying individuals with an increased family history and making a referral to one of four cancer genetic services in Scotland.

General Practitioners and Family history risk assessment.

The Scottish service proposal for individuals with a family history of cancer is slightly different than that proposed in a recent Government report for England and Wales (NHS 2003). This report proposes that it is the role of a GP, surgeon or oncologist to take a detailed family history, make an assessment of family history risk and a decision to discharge, screen or refer to cancer genetic services.

In Scotland, the model implemented requires GPs, surgeons and oncologists to assess family history risk and make a decision to refer to cancer genetic services.
Before the proposed Scottish model was implemented, Fry et al (1999) had shown that only 6% of GPs in SE Scotland felt confident on giving a risk based on family history. This highlights the requirement of an education programme for GPs in assessing family history using Scottish guidelines. When the Scottish cancer subgroup report was published it recommended a roll out programme of education to primary care, general surgeons, oncologists, gastroenterologists, radiologists and gynaecological oncologists in all NHS trusts in Scotland. Also, relevant bodies responsible for training of medical students, qualified medical staff and paramedical staff should ensure a planned programme of ongoing education. This report stated that the Health Department would

provide further guidance for these activities to be set in place. These Scottish guidelines for breast, ovarian and colorectal cancers were issued to GPs in April 2002.

The important topic of GP involvement in cancer genetics is only beginning to appear in the literature. It has been agreed by GPs that they have a role to play in cancer genetics (Fry et al 1999, Suchard et al 1999) although there is little agreement as to what that role should be or how the service for cancer genetics should develop (Watson et al 1999, Suchard et al 1999). There is also a lack of understanding by GPs on what the cancer genetic services can provide for individuals with a family history of cancer (Watson et al 2001).

Many studies identified that GPs had a problem with knowing when an individual should be referred to a cancer genetic service (Fry et al 1999, Suchard et al 1999, Rose et al 2001).

GPs have identified that they do not see many individuals with a family history of cancer in their day to day practice.

A GP would expect to have approximately 60 patients with a family history of a common cancer, for each 1000 patients, aged 30-69 (House et al 1999). With the volume of patients seen by GPs on a daily basis, 60 patients is a relatively small number to remember to use guidelines. This highlights the need for easy accessible and user friendly guidelines, especially as they are not being used on a daily or even a weekly basis.

Although GPs have said, that guidelines and computer aided guidelines would be helpful to them for assessing family history (Watson et al 2001), Rose et al (2001) reported less than one third of a GP study cohort was aware of family history guidelines which had been sent to them.

Suchard et al (1999) found that the number of patients discussing family history concerns is already affecting GP workload, and they feel that there is a lack of time to enable a detailed family history to be taken within an average GP consultation which takes approximately 8.5 minutes.

In many of the studies carried out to assess GPs perception of their role in cancer genetics the majority of GPs indicated that they need more education in genetics and assessing family history risk. Studies suggested that the practice nurse could be offered training on taking a detailed family history or that a genetic nurse specialist could be involved with GP practices (Fry et al 1999, Watson et al 1999, Rose et al 2001, Johnson et al 1995, Summerton & Garrod 1997). It is clear further research is required to offer the optimum service to individuals with a family history of cancer. As the general public are now more educated in health issues the demand for information on family history risk will become greater.

Lucassen et al (2001) found that when GPs were provided with an educational pack which included guidelines, the number of appropriate referrals improved and the quality of referral letter which enable the genetic service to assess the risk to triage for appropriate appointments.

More general studies on changing behaviour of GPs have found that if education is offered it should have enabling or reinforcing strategies or there is little impact on GP behaviour or performance. Change is more likely if the education package is based on needs assessment, uses case histories, allows time for discussion, is well evaluated and is facilitated by a GP (Davis & Taylor-Vaisey.2000). In addition, (Wensing & Grol 1994) reported a combination of interventions such as peer review; feedback to GP and individual instruction all appear to have greater impact on changing behaviour and practice.

Other health care professionals and family history risk assessment

Summerton and Garrod (1997) suggest it is unrealistic for GPs to carry out family history taking. They propose that practice nurses (PN) or health visitors (HV) could be trained to do this and simple application of a sticker to patients' notes would alert a GP to the presence of a family history of disease. In a study carried out by Bankhead et al (2001) to investigate genetic knowledge of practice nurses found that 96% stated that they take family history as routine and 61.5 % had been asked a family history question in relation to family history of cancer, in past 3 months. Many practice nurses saw their role as 'giving permission' to the patient to discuss their family history with the GP, very few referred the patient on to the GP for advice and/or referral to cancer genetic services. Bankhead et al (2001) found practice nurses over estimated family history risk in both breast and colorectal cancer, more so the latter where 89.5 % of the practice nurses overestimated the risk, using a scenario. Chorely and McDermont (1997) investigated senior doctors and nurses involved in all areas of cancer care and used a questionnaire to ask information on cancer genetic knowledge. This small survey showed an obvious dichotomy between wanting to provide information for future management and having the ability to do so. They found family history was not discussed due to lack of time, the criteria for testing and surveillance were not used and staff did not appreciate the wider issues such as impact on individual patients, their families and the need for confidentiality.

Collecting cancer family history

Large epidemiological studies for common cancers reported 'family history' as a risk factor. The Nurses Health study (Colditz et al 1993) and Utah Population database

(Slattery et al 1993) reported on breast cancer; the Utah population database (Slattery et al 1994) on colorectal cancer.

With family history identified as a risk factor for colorectal cancer some researchers have recorded family history as part of their core dataset. However, these studies had a main aim of validating the accuracy of family history cancer information reported. Also, the methodology for collecting family history varies within the studies. Table 10 summarises the studies, which have collected family history data regarding colorectal cancer as a part of their research study.

Table 10 Studies with the main aim of assessing the accuracy of the family history information given by the study subject

Author. Country. Year of publication	Number of cases and controls	Year of data collection. Age criteria. Degree of kinship collected	Method of collecting family history	Accuracy[8] of reported cancer and cancer site by case.	Percentage of reported cancers confirmed. Method of validating family history	Main points
Love USA 1985	121 individuals attending CGC 16 M - 105 F	1981 23-75 All degree	Face to face interview by geneticist	93% Colorectal cancer accuracy of reporting in FDR 84% Colorectal cancer accuracy in SD and TDR 70% accuracy for all other cancers including endometrial and ovary 17.1% over-reported	90% FDR, 65% SDR, 49% TDR Confirmed by: DC, P, OP, AR, DS,	FDR reports are most accurate Proband self referred and possibly more highly motivated 35 cancers found not reported in FDR & SDR, higher numbers found not reported in TDR Predominantly more females than males
Kee and Collins Ireland 1992	100 individuals with colorectal cancer	1990 55-74 All FDR	Face to face by a trained interviewer	57 % overall accuracy in reporting colorectal cancer cases	94% cancers confirmed MR, P, CR, DC	Proximal tumours no more likely to have a positive F/H than distal tumours
Aitken Australia 1995	380 with adenoma or polyps 1096 controls no adenoma or polyps	1980-85 20-75 All FDR	Self administered questionnaire	77.8% accuracy for colorectal cancers 98% Accuracy for those reporting no cancer f/h 22.2% over-reported	51.8% cancers confirmed OD, MR, DC	Accuracy increased with age, females and those with private health insurance

8 Accuracy of family history is: how accurate was the information given by the case when confirmed by another method e.g medical notes or pathology.

Author. Country. Year of publication	Number of cases and controls	Year of data collection. Age criteria. Degree of kinship collected	Method of collecting family history	Accuracy[8] of reported cancer and cancer site by case.	Percentage of reported cancers confirmed. Method of validating family history	Main points
Glanz Hawaii 1999	426 Siblings or adult child with a FDR with colorectal cancer	1987-1996 19-84 All FDR	Self administered questionnaire	74.6% Accuracy in reporting colorectal cancer in FDR 25.4% underreporting	All FDR with colorectal cancer of these cases were known to the research study	Females more likely than males to know diagnosis in FDR. High knowledge score, cancer worry, higher perceived risk, greater cancer Stage Are more likely to report FDR with colorectal cancer
Douglas UK 1999	400 Newcastle 195 Manchester Proband referred to CGC	1994-95 all ages All degree	Face to face interview with geneticist	Centre 1 – 86% accuracy for all cancer sites in FDR Centre 2 – 94% accuracy for all cancer sites in FDR Combining both centres data 90% accuracy in reporting colorectal cancer and 83% ovarian cancer 15.3% over-reported	42% Reported cancers confirmed MR, P, CR, OD, OGD	More accurate in FDR 17 cases did not report second primary Recommend use of cancer registries Many more Females than males
Sijmons Netherlands 2000	139 Proband referred to CGC	1977-97 All ages All degree	Questionnaire pre appointment and Face to face interview with geneticist	95% Overall accuracy Colorectal cancer accuracy 89% all deg 42% accurate for Uterine cancer	43% cancers confirmed MR, P	Differences between degrees of relative small. Multiple primaries 94% accurate

Author. Country. Year of publication	Number of cases and controls	Year of data collection. Age criteria. Degree of kinship collected	Method of collecting family history	Accuracy[8] of reported cancer and cancer site by case.	Percentage of reported cancers confirmed. Method of validating family history	Main points
Church & McGannon Ohio 2000 Accuracy of recording in MR	100 in 1993 96 in 1997 Case had colorectal surgery	1993 and 1997 All ages FD& SDR	Active medical chart and detailed interview	Family history was assumed as correct.	80% in 1993 74% in 1997 Accuracy of colorectal cancer in medical records against detailed family history taken at interview.	No record of who recorded family history Study repeated after 4years and staff undergone education accuracy of reporting was lower
Katballe Denmark 2001	1328 cases with colorectal cancer	1995-97 All ages All FD and SDR with cancer under 50	Interviewed by surgeons using a questionnaire as guide	81.7% accuracy in reporting colorectal cancer	83.7% cancers confirmed MR, P, AR, DC	Proband to CGC more accurate than unselected cases. Recommend verification if surveillance or testing to be offered.
Rou USA 2001 Limitation of taking F/H at surgical consultation	125 with colorectal cancer 54 M & 71 F	1986-97 40 or under All FDR	Initial MR and subsequent telephone administered questionnaire	N/A	N/A	4.8% HNPCC families Proband all under 40. At surgical consultation 78% of cases had F/H documented of these 39cases low risk after telephone interview 22 (56.4%) upgrade to higher risk

Author. Country. Year of publication	Number of cases and controls	Year of data collection. Age criteria. Degree of kinship collected	Method of collecting family history	Accuracy[8] of reported cancer and cancer site by case.	Percentage of reported cancers confirmed. Method of validating family history	Main points
Olsson & Linblom Sweden 2003	411 with colorectal cancer	1998-2001 45-74 FDR, SDR, TDR	Questionnaire form, then face to face with trained interviewer	N/A	95% confirmed P, DC, MR	1.2% HNPCC family histories.
Mitchell Scotland 2004	199 colorectal cancer cases 86F 113M Controls 133	Year not reported Mean age for cases 64 years and controls 64.2 years FDR & SDR	Face to face interview by a genetic nurse	CASES 44% FDR 14% SDR All cancers accuracy CONTROLS 41% FDR 18% SDR 55.7% colorectal cancer	89% cases 91.5% controls CR	Trend towards more accurate reporting in recent years. 40-50% underreporting. No difference between cases and controls, no effect of age or sex. Disparity between FDR & SDR

Table 10 Abbreviations: **FDR**-first degree relative, **SDR**-second degree relative, **TDR**-third degree relative, **CGC**-cancer genetic clinic, **FH**-family history, **F**-female, **M**-male, **P**-pathology, **MR**-medical records, **DC**-death certificate, **OD**-own doctors records, **OP**-operation notes, **DS**-discharge summary, **AR**-autopsy report, **CR**-Cancer registry, **OGD**-other genetic department.

Table 11 Comparison of studies assessing risk for individuals within a family with colorectal cancer

Author. Country. Aim of study. Year of publication	Number of cases and controls	Year of data collection, Degree of kinship collected	Method of collecting family history	Reported risk with family history definition	Accuracy of reported cancer and cancer site by case.	Percentage of cancers validated and method of validating family history	Main points
Slattery USA 2003	1055 colorectal cancer cases Controls 1304	1997-2001 30-79 All FDR	Questionnaire completed by trained interviewer	Risk with a FDR <50 2.09 Rectal 3.00 Distal 7.88 Proximal	N/A	No confirmation of family history	Reporting on risk association with FDR with colorectal cancer.
Andrieu France 2003	766 colorectal cancer cases	1993-1998 All ages All FDR and SDR	Questionnaire completed by trained interviewer	Relative risk F 1.72 >70 M 1.46 >70	79.1% all degree accuracy. 87.5% FDR accuracy colorectal cancer	78% CR, MR, OD, P.	Offered relative risk and colorectal cancer family history for gender and age

Table 11 Abbreviations: **FDR**-first degree relative, **SDR**-second degree relative, **F**-female, **M**-male, **FH**- family history, **OR**-odds ratio **FP**-pathology, **MR**-medical records, **DC**-death certificate, **OD**-own doctors records, **CR**-Cancer registry, **OGD**-other genetic department.

The studies shown in Table 10 all confirmed the accuracy of the family history information given by an individual. Table 11 shows studies that used the family history information given by an individual to assess population or relative risk for an individual of developing colorectal cancer.

The studies in table 10 include studies from UK, Europe and USA. Within theses studies there are a variety of methods used to collect family history.

There are different cohorts in these studies. These include individuals with colorectal cancer, individuals attending a cancer genetic centre with a family history concern and individuals with a known first degree relative with colorectal cancer. The majority of these studies had no age restriction for eligible participants. Within the studies a variety of family history data were collected. Four studies collected only first degree relative information, three studies collected information on first degree and second degree relatives and three studies collected information on all degrees of relatives. The latter cancer genetic studies were specifically in which it is mandatory to take a minimum three generation family history.

There is no literature to inform the most effective method of collecting an accurate family history. Theis et al (1994) did note a small added benefit in accuracy of cancer site when family history was taken by a trained genetic nurse. Koscica et al (2001) found that utilising a genetic counsellor and incorporating a three-generation pedigree into a patient's risk assessment significantly improved detection of identifiable genetic risk factors.

Results from all of the studies in table 10 showed that the accuracy of family history information was significantly greater in first degree relatives and became less accurate the further removed the relative was from the consultand. The studies carried out in cancer

genetic centres had a higher degree of accuracy in first degree relatives than the other studies. This may be explained by the fact that the individuals in the study are likely to have raised the family history concern with their GP and are highly motivated to find out family history information.

Also of interest is that in the cancer genetic studies there were a higher proportion of females and these females give more accurate family history information than males in the same studies.

Accuracy of family history data

A Consultand[9] attending a cancer genetic clinic is given important information based on family history reported; this family history information influences:

- Risk assessment
- Counselling
- Surveillance
- Genetic testing

If the initial family history information given is incorrect, all subsequent information based on the family history will be incorrect. Several authors in table 10 have described the accuracy of the reported malignancy in relatives, there are, however inconsistencies within these studies in the methodology of confirming cancers.

Family histories of breast cancer have consistently been found to have a high degree of accuracy when the information was confirmed with cancer registries or medical records (Theis et al 1994, Anton Culver et al 1996). Love et al (1985) studied 121 consecutive people referred to a genetic clinic with a family history of cancer. The results showed 93% accurately reported colorectal cancers in first-degree relatives, dropping slightly to 84% for second and third degree relatives. An accuracy of 70% was given for other HNPCC related cancers which included ovarian and endometrial cancer.

In recent studies, Douglas et al (1999) and Sijmons et al (2000) reported on cancer family history referrals to genetic clinics. Douglas et al (1999) compared, two UK centres and found the overall accuracy for all cancers reported in first-degree relatives was 86% (centre 1) whilst in centre 2 the accuracy was 94%. In centre 2 a 90% accuracy of

9 The person being seen in a clinic for genetic counselling

colorectal cancers were reported and an 83% accuracy of ovarian cancers reported. Sijmons et al (2000) reported similar results in their study; they reported 89% accuracy for colorectal cancers reported and 71% for ovarian cancer, in all degrees of kinship.

Aitken et al (1995) reported a 77% accuracy of colorectal cancer information in first-degree relatives of individuals with adenomas found at colonoscopy. Glanz et al (1999) found adults with a first degree relative diagnosed with colorectal cancer, were 74.6% accurate in reporting colorectal cancer. Katballe et al (2001), Andrieu et al (2003) and Mitchell et al (2004) all reported on family history information accuracy from individuals diagnosed with colorectal cancer. Katballe et al (2001) identified 81.7% accuracy of reporting colorectal cancer, in all first and second-degree relatives. Andrieu et al (2003) reported accuracy of 79.1 % in all degrees of relatives, which was increased to 87.5% when only first-degree relatives were considered.

However, Mitchell et al (2004) reported significantly less accuracy for all cancer sites, they reported 44% accuracy in first-degree relatives and 14% accuracy in second-degree relatives. They also gave the results on accuracy of colorectal cancer reported in relatives; the accuracy in first-degree relatives was found to be 56% and accuracy of reported colorectal cancers in second-degree relatives was 29.5%.

Some studies reported on the underreporting of cancers which were found when investigation the family. Mitchell et al (2004) and Glanz et al (1999) both found under reporting of cancers in first-degree relatives at 24.5% and 29% respectively. In contrast, Love et al (1985), Aitken et al (1995) and Douglas et al (1999) found an overestimation in cancer reports at 17.1%, 22.2% and 15.3% respectively. Aitken et al (1995) and Katballe et al (2001) both reported cases to be more accurate than controls. It was

thought, that a diagnosis of colorectal cancer or adenoma was the catalyst that prompted them to seek more information on family history and they were more enthusiastic about sharing this information. However, Mitchell et al (2004) in a Scottish study found no difference between cases and controls in accuracy of cancers reported. Glanz et al (1999) and Aitken et al (1995) both reported that females were more accurate at reporting cancers in the family than males. Aitken et al (1995) also reported that increased age was positively related to the degree of cancer site accuracy. Many of the above studies also reported a striking drop in accuracy with increasing distance of relationship from the person giving information. Love et al (1985) suggested that those seen within genetic departments are more motivated than colorectal cancer cases within a research study because they sought referral or were advised to have a referral to discuss their family history concerns. All of the investigators reported that the time factor and the cost of confirming information required careful consideration when developing a research study or cancer genetic service. Access to information that could confirm the accuracy of the family history was a problem for several of the studies. Difficulties experienced were in accessing records due to:

- Inability to obtain consent from case or next of kin,
- Destroyed hospital files
- Closed hospitals

The validation of the cancer information given by cases and controls varied from 95% in a Swedish study (Olsson & Linbolm 2003) to 42% reported in a UK study (Douglas et al 1999).

Genetic information and professions allied to medicine

The field of cancer genetics is developing almost daily with new knowledge and advances in technology, and this new information is now reaching the public domain at the same time as it is available in the medical literature. It is difficult for GPs and surgeons to stay current with new information. Although many GPs and surgeons may be willing to take a detailed family history, the time factor and lack of education on the genetics of common diseases are barriers to the development of cancer genetic services in primary care (Kinmonth et al 1998 and Fry et al 2001).

Recent literature concludes that asking family history information is not the sole responsibility of GPs, surgeons and oncologists as previously proposed. This knowledge and skill should be integrated into the role of all health care professionals.

The white paper 'realising the potential of genetics' NHS (2003) stated:

> *"Over time most health professionals will need to understand how a patient's family history and genetic make-up affects the likelihood of developing a disease or their response to medicines. They will need an appreciation of how genetic technology can be used in diagnosis, prevention and treatment. They will need to be able to convey this information to patients and help them make difficult choices about whether to undergo genetic testing or to change lifestyle in the light of information about their genetic make-up" (p47)*

Specialist genetics centres will be required to play a role in the diffusion of new genetic information across all professions within the NHS. The suggestion has been made that genetic counsellors could be attached to primary care areas to assist with the transfer of information and skills required to take family history and assess family history risk (NHS 2003). However, Public Health Genetics Unit (2002) reports that education systems for dissemination of this information are not currently available. A rolling programme of educational resource development must be implemented, covering all levels of each professional group based on an understanding of needs and priorities.

If all health professionals had the skill to take a family history and assess risk, they would have sufficient knowledge to make a referral of those with a moderate and high-risk family history to genetic centres. This would reduce the workload of cancer genetic clinics (Wondering et al 2001 and Campbell et al 2003), improving the waiting times for moderate and high-risk patients.

General population cancer family history knowledge

Despite heightened media attention surrounding the human genome and the impact this new knowledge has had on cancer genetics, the general population does not appear to use this knowledge to assess their own family history risk or to access appropriate services. Cull et al (2001) found that 44% of women attending an ovarian cancer clinic underestimated their risk and 19% overestimated their risk. To achieve a satisfactory level of understanding of one's own family history risk and how to deal with this concern, will require less sensationalism from journalists and easy public access to printed media to increase awareness and understanding (NHS 2003).

Todara et al (2001) carried out four focus groups, with a small number of individuals aged 30-69; each had a first-degree relative with colorectal cancer. None of the four groups had heard of a genetic risk assessment. There was concern surrounding, the effort it would take them to collect family history information. This study and Lynch and Lynch (1996) found that fear of losing or loading of insurance coverage was another barrier to personally accessing genetic services.

In the past, there has been limited patient and family information published by cancer charities offering guidance on the family history of colorectal cancer. However, new

information leaflets are now available with more specific information on family history (Beating Bowel Cancer 2003, CancerBACUP 2004) A recent publication by Cetnarskyj (2004) offers information to individuals in Scotland who have a concern regarding their family history of colorectal cancer (*Appendix 7*).

A major problem for the dissemination of family history information as a risk factor is that individuals normally contact these charities when they have colorectal cancer and find out they should have been screened regularly prior to their diagnosis.

Summary of family history

There is little current literature regarding individuals with colorectal cancer and their family history of colorectal cancer. There are no published data on the number of individuals with an increased family history risk in the Scottish colorectal cancer population.

There is no published literature on those that perceive they have a family history of colorectal cancer and present with lower gastrointestinal symptoms or how they perceive their symptoms on the background of their family history of colorectal cancer.

Other Risk Factors for Colorectal cancer

Colorectal cancer is a multi-factorial disease, with complex interactions between genetic and environmental factors. A small number of individuals are at a much higher risk of developing cancer due to known and yet unknown gene mutations in their family.

There are several other environmental factors thought to contribute to an individual's risk of developing colorectal cancer in addition to family history. These are:

- Dietary factors
- Excess Weight
- Physical activity
- Smoking
- Alcohol

The above risk factors will not be discussed further in the thesis, as it would not be possible to offer a succinct overview due to the vast literature in this area.

Chapter 6

Socioeconomic Status and Colorectal Cancer

Socioeconomic status and 'inequalities in health'

For many years, there has been an awareness that a relationship between poverty and mortality risk exists. Today, inequality in health between the affluent and the deprived is high on the political agenda. Monitoring inequality in health has become an increasingly important task of development agencies.

This inequality in health has not always been recognised by the government. However, not only are these inequalities unfair, they are also an economic burden. Improving health in disadvantaged groups would improve the health status of the population.

The Black report (Townsend 1988) identified higher morbidity and mortality in deprived areas compared to more affluent parts of the UK, thus bringing the problem to the forefront of the social and political agenda. Government and Health Boards now openly accept and discuss the concept of inequalities in health. The lessening of inequalities in health and the promotion of equity in access to health care are now central to the UK government's Health policy (Department of Health, 1998).

One of the major principles of the National Health Service (NHS) was to provide equal treatment for equal need free at the point of delivery. However, private practice was allowed to coexist with the NHS inevitably contributing to inequalities in health care between the rich and poor (Secretary of State, 1998). More than 50 years have passed since the beginning of the NHS and most health services remain free at the point of contact. However there is clear evidence that the gap is widening in health between the affluent and the deprived (Phillimore et al 1994, Davey Smith et al 1998).

This is an international problem that all governments are aiming to address. A target issued by the World Health Organisation in 1990 stated,

> *"By the year 2000, the differences in health between countries and between groups within countries should be reduced by at least 25%, by improving the level of health of the disadvantaged nations and groups"*
>
> (WHO, 1990)

This was a very ambitious target for many countries to meet and could not be met in many areas of medicine. This target has driven many researchers to investigate discrepancies in care within their own area of health that has provided many useful insights into inequalities in health for those individuals living with poverty and deprivation.

In the field of cancer medicine, professionals have embraced this challenge and have begun the development of more accurate recording and collaboration with other countries. The EUROCARE project is one such collaboration to develop from this challenge. The role of EUROCARE is to collate and disseminate cancer statistics in Europe.

Poverty and deprivation

The terms poverty and deprivation are difficult to define; they are often used interchangeably when discussing those who are underprivileged in some way. It has been argued, that there is a clear distinction between poverty and deprivation, Townsend (1987b) wrote,

> *"Deprivation may be defined as a state of observable and demonstrable disadvantage, relative to the local community or the wider society or nation to which an individual, family or groups belong"*

A further attempt to distinguish poverty and deprivation was made by Noble et al (2000);

> *"It can be asserted that the condition of poverty means not having enough financial resources to meet needs. Deprivation on the other hand, refers to unmet need, which is caused by a lack of resources of all kinds, not just financial."*

Townsend would not agree with these separate definitions;

> *"While people experiencing some forms of deprivation may not all have low income, people experiencing multiple or single but very severe forms of deprivation are in almost every instance likely to have very little income and little or no resources".*

Further to the definitions of poverty and deprivation given, Townsend (1987a) elaborates on the distinction between 'social' deprivation and 'material' deprivation. Social deprivation he feels is more difficult to measure and is defines as;

> *"Providing a useful means of generalising the condition of those who do not or cannot enter into ordinary forms of family or other relationships"*

Today, this is better known as social exclusion. He stated that to measure material deprivation was a much easier task as it relates to diet, health, clothing, housing, household facilities, environment and work.

However poverty or deprivation is interpreted, they are a measure of social standing and often referred to as socioeconomic status. Mackenbach and Kunst (1997) gave the following definition of socioeconomic status:

> *"Socioeconomic status refers to an individual's relative position in the social hierarchy and can be operationalised as a level of education, occupation and/or income"*

Throughout the literature deprivation and poverty are also reported as socioeconomic status and the term socioeconomic status will be used within this thesis to define the differences between individuals in higher or lower social groups.

Measures of deprivation

Throughout the literature there are various instruments used to measure socioeconomic status, each author choosing the best method available for the population they are studying. The measurement tool used is also determined by the available access to the required information. Also the tool will be determined by the relevance of each indicator with respect to the culture of the population studied.

Census-based material is the most common source of data used to calculate socioeconomic status, as access to these data is readily available (Kogevinas et al 1991, Schrijver et al 1995, Mandelblatt et al 1996, Kee et al 1992, Ionescu et al 1998, Pollock and Vickers 1998, Kim et al 2000, Campbell et al 2000, Brewster et al 2001).

Although not explicit in their text, it appears that other authors use data from their own official National sources equivalent to the Office of National Statistics in England to assess socioeconomic status (Brenner et al 1991, Desoubeaux et al 1997). Some countries have the ability to link census data to personal records, which can then be accessed for research (Auvinen 1992). A small number of studies have collected the socioeconomic information they require at recruitment (Tavani et al 1999, Ciccone et al 2000). Alternatively a combination of census and personal information is used (Lynch et al 1975).

The variables used from census data vary greatly in each study. Table 12 illustrates the socioeconomic variables used by researchers, the country of the research, the study population and the period of data collection.

Table 12 Variables used as a measure of socioeconomic status

Author	Year of Study	Country	Study population	Data Collection time (in years)	Socioeconomic status information
Lynch	1975	Nebraska, USA	Colorectal cancer cohort from 11 hospitals	1	Educational status, occupation and mean income from census
Papadimitriou	1984	Greece	Case control from two hospitals	1.5	Personal interview breakdown not given
Kogevinas	1991	London,	OPCS study.	10	Housing tenure
Brenner	1991	Saarland, Germany	Cancer registry, colorectal cancer cohort	9	Mean number in household, residential area, proportion of Catholics, proportion with no more than 9yr school education
Kee	1992	Ireland	Cancer registry, colorectal cancer cohort	1	Townsend deprivation index – census based
Auvinen	1992	Finland	Cancer registry, colorectal cancer cohort	3	Social class from personal records in census
Monnet	1993	France	Cancer registry colorectal cancer cohort	4	comfort of housing, census based
Faggiano	1994	Italy	All cancers in a population	3	Social class, Education levels
Van Loon	1995	Netherlands	The Netherlands cohort study	1	Educational level, occupational history,
Schrijver	1995	Thames region, UK	Cancer registry colorectal cancer cohort	2x5	Carstairs deprivation index - census based
Mandelblatt	1996	New York, USA	Cancer registry colorectal cancer cohort	5	% below poverty level and % unemployed – census based
Desoubeaux	1997	France	Cancer registry colorectal cancer cohort	9	Occupation & distance from nearest specialist health care centre

Author	Year of Study	Country	Study population	Data Collection time (in years)	Socioeconomic status information
Pollock and Vickers	1998	Thames region, UK	Cancer registry colorectal cancer cohort	3	Townsend deprivation index – census based
Ionescu	1998	Tayside, Scotland	Pathology reports from one hospital.	6	Carstairs deprivation index - census based
Tavani	1999	Italy	Case controls in one-year, in six areas	2x5	Social class by head of household occupation – census based
Ciccone	2000	Italy	Colorectal cancer cases from one hospital.	1	Occupation history and educational level by personal interview
Campbell	2000	Scotland	Diagnosed with colorectal cancer from Cancer registry.	2	Carstairs deprivation index - census based (see below)
Kim	2000	Lancaster, UK	Wessex cancer database	Not given	Carstairs deprivation index - census based
Polendak	2001	Conneticut	Cancer registry colorectal cancer cohort	1	Poverty rate and residence tract – census based
Brewster	2001	Scotland	Cancer registry colorectal cancer cohort	4	Carstairs deprivation index - census based
Hole and McArdle	2002	Greater Glasgow, Scotland	Colorectal cancer patients from eight hospitals.	3	Carstairs deprivation index - census based
Wrigley	2003	Wessex health region, UK	Wessex colorectal cancer Audit, diagnosed	1	Townsend deprivation index – census based

The above table demonstrates the many differences between research studies which can create difficulties when comparing results. The most common measures of deprivation used are Carstairs and Townsend deprivation indices, especially in the United Kingdom. These are discussed in more detail below.

Deprivation indices

Deprivation indices are widely used within epidemiology and public health research. These indices are based upon the characteristics of the area of residence at the time of census. These indices are most often used when data relating to socioeconomic status have not been or cannot be directly collected during a study. Since the early 21st Century, there have been many attempts to produce deprivation indices of relevance to socioeconomic status.

The two indices most frequently used in cancer research in the UK are the Townsend index and the Carstairs index. These are strongly correlated to each other as they measure similar factors contributing to deprivation (Morris et al 1991). The score derived from these indices are updated with each census and current scores available for each index incorporate 2001 census data, this is available on the World Wide Web, the Carstairs index (www.scotland.gov.uk) and Townsend index (www.wales.nhs.uk).

There has been some criticism of census-based measures as data may be out of date soon after it is published (Majeed et al 1995). There are also worries about how the data from census should be interpreted. Many individuals in employment have a level of pay that is low but does not allow access to social security benefits. Their socioeconomic status, measured by these indices, is wrongly assessed (Beale, 2001). Beale (2001) also argues against the use of car ownership as an indicator of affluence, since in rural areas a car is an absolute necessity. In many rural areas, the most affluent group and the most deprived group live within a small area, which could be covered by the same ward or postcode.

A new measure of deprivation has recently been developed for UK nations and does not rely on census data. This index attempts to measure multiple deprivation indicators and produce a more dynamic index that has the ability to change more frequently than census data also, to assess more accurately socioeconomic status.

This new deprivation index incorporates many more indictors of deprivation than are currently used in either of the Townsend or Carstairs indices. Scotland, England, Ireland and Wales have each tailored the indicators used in their index to reflect the known areas of deprivation within their own region. The Scottish index is called the 'Scottish Index of Multiple Deprivation' (SIMD 2003). At the time of writing none of the four new multiple deprivation indices have been validated due to their recent publication. This study will use both the SIMD index and the Carstairs index for analysis and will compare results.

Townsend Deprivation index

The Townsend Index is a composite census based index, which originated from the 1981 census data. It measures multiple deprivations by small areas known as wards, and incorporates four variables:

- Unemployment - (lack of material resources and insecurity),
- Overcrowding - (material living conditions),
- Lack of owner occupied accommodation - (a proxy indicator of wealth)
- Lack of car ownership - (a proxy indicator of income).

(Townsend et al 1988)

Calculating the Townsend deprivation score

The Townsend score is a sum of the standardised scores (z scores) for each variable; scores greater than zero indicate greater levels of material deprivation. These scores are available for England, Wales and Scotland for this index.

The index score is calculated by combining four variables from the most current census data available (the higher the number, the greater the measure of deprivation):

- Unemployment - unemployed residents over 16, as a percentage of all economically active residents aged over 16.
- Overcrowding - households with 1 person per room and over as a percentage of all households.
- No car ownership - households with no car, as a percentage of all households.
- No home ownership - households not owning their own home, as a percentage of all households.

Carstairs Deprivation index

The Carstairs deprivation index originated in 1981 and was created by Carstairs (1982). It is a composite census-based index based upon postcode areas and incorporates the following 4 variables from the 1981 population census,

- Overcrowding,
- Male unemployment,
- Low social class (population with social classes 1V &V of the Registrar General's social class)
- Households with no car.

(Carstairs, 1982)

These four variables are intended to represent the materially disadvantaged. The scores were revisited with the 1991 census and the same variables were used. Slight changes were made in definition of overcrowding and social class in view of the Registrar General's switch to an occupational basis. It was concluded that there was no substantial change in the scores for most areas in the 10-year period between 1981 and 1991; those areas that did show a change were more likely to have a population of less than 2000.

The 2001 Carstairs score have been derived from the same four variables used in the 1991 score. The social class score was no longer available due to a change in Registrar General reporting. Special tables were commissioned from the census division of the General Register Office for Scotland, to maintain as closely as possible that the same four variables used for 1999 scores (McLoone 2003). There was little change in the score over the ten-year period from 1991 to 2001.

Calculating the Carstairs Deprivation score

The scores were derived from an unweighted combination four standardised variables giving a summary statistic (Z score) for an area.

- Overcrowding - The proportion of all persons living in private households with a density of more than one person per room
- Male unemployment - The proportion of economically active males seeking work
- Low social class - Proportion of all persons in private households with head of household in social class 4 or 5
- No Car - proportion of all persons in private households with no car

Using these four variables and postcode area, a score is calculated; this score is commonly known as the Depcat score. A postcode is available for every address in the UK and is commonly used in the recording of births, deaths, and marriages and is widely used throughout the health service for hospital admissions, discharges and similar events. Postcodes consist of an area of postal delivery, which in residential areas consists of approximately 35 people. The postcode is sectioned into area, district, sector and unit. The analysis for the Carstairs Depcat score is at the sector level, which is thought to provide reasonable reliability in respect of most health events (Carstairs and Morris 1991).

Scottish Index of Multiple Deprivation 2003

This Scottish Index of Multiple Deprivation (SIMD) (Social Disadvantage Research centre 2003) does not use census data, unlike Townsend and Carstairs. The score for this index are given at ward level but it is possible to convert to postcode areas through a conversion file from General Registrar's Office. This index consists of separate domains of deprivation, each with its specific information. The domains used in the SMID 2003 are:

- Income deprivation,
- Employment deprivation,
- Health deprivation and disability;
- Education, skills and training deprivation,
- Geographical access to services.

Each domain reflects a particular aspect of deprivation and the purpose of each domain is as follows:

- Income - to capture the extent of income deprivation in an area
- Employment – to measure enforced exclusion from the world of work
- Health deprivation and disability – to identify areas with high proportion of people who are losing years of life due to premature death or whose quality of life is impaired by poor health
- Education, skills and training deprivation – to measure as consistently as possible the key educational characteristics of the local area that might contribute to the overall level of deprivation and disadvantage
- Geographical Access to services – to measure the extent to which people have poor geographical access to key local services.

Within each domain, there are specific measures, for example; the Health deprivation and Disability indicators consists of:

- Comparative Mortality factors for under 75s
- Hospital episodes related to alcohol use
- Hospital episodes related to drug use
- Comparative Illness Factor
- Emergency admission to hospital
- Proportion of the population being prescribed drugs for anxiety, depression or psychosis
- Proportion of live singleton births of low birth weight.

Calculating the Scottish Index of Multiple Deprivation score

The score is a composite of the different domains of deprivation, each dimension is measured independently using the best indicators available. These domains are combined

with explicit weighting to generate a Scottish Index of Multiple Deprivation (SIMD), which is an average of the component domains. The scores in this index are cumulative for all sections of the index and range from 1- 89, including two decimal points, 1 being the most affluent and 89 being the most deprived.

Socioeconomic status, incidence and colorectal cancer

The specific causal factors of deprivation that are important for survival from colorectal cancer remain elusive.

England and Wales

There was no difference in the incidence of colon cancer in either sex related to deprivation as measured using Townsend deprivation index. A clear influence of deprivation was noted in males with rectal cancer when a 25% increase in incidence in the more deprived groups was seen.

The picture for mortality mirrors the incidence. There was a 50% higher mortality rate for males with rectal cancer in the most deprived group than for males in the most affluent group (Quinn et al 2001). This effect was not seen in females.

Scotland

All current ISD publications use Carstairs index 1991. Of those diagnosed with colorectal cancer in 1997, there were 43% in the most affluent group and 36% from the most deprived group for both colon and rectal cancer. The distribution of age at diagnosis was similar for colon and rectal patients across the deprivation groups, with a median age of 73 years. The incidence of colon cancer was 8% higher in the most

affluent group compared to the most deprived group; the same pattern was seen for rectal cancer with a smaller gradient (Stockton 2001).

The incidence of colorectal cancer has also been reported to be higher in the most affluent group (Lynch et al 1975, Brenner et al 1991, Faggiano et al 1994, Schrijvers et al 1995, Kee et al 1996, Tavani et al 1999, Ciccone et al 2000, Hole & McArdle 2002). This mirrors deprivation gradients reported from many cancer registries, although many of the studies cited use different measures of deprivation. Faggiano et al (1994) in an Italian study suggested that the lower incidence of colorectal cancer in the most deprived group was associated with a lower fat and higher fibre diet than more affluent group.

Papadimitriou et al (1984) and Kim et al (2000) found that there was no trend towards higher incidence in the most affluent group. Auvinen et al (1992) found that the incidence was higher in the most deprived group, using social class as the measure of deprivation where census records were linked to personal files, perhaps a better indicator of individual socioeconomic status.

Tavani et al (1999) noted an increase in colorectal cancer in the affluent group using social class as the measure of socioeconomic status and also noted that this increase was less for rectal cancer. Schrijvers et al (1995) found the opposite from Tavani, where a 9% increase in rectal cancer and a 5% increased in colon cancer incidence in the deprived group versus the affluent group. With a greater proportion of studies reporting an increased incidence of colorectal cancer, it implies that there is an association with increased incidence and socioeconomic status, therefore suggesting that a proportion of colorectal cancer may be preventable (Kee et al 1996).

Socioeconomic status and survival from colorectal cancer

England and Wales

There was an obvious difference in survival rate and socioeconomic status for both colon and rectal cancer in those diagnosed in 1986-90. In the most deprived group one-year survival for colon cancer was 6% less and 7% less for rectal cancer than the most affluent group. Five-year survival for colon cancer was 4% less in the most deprived group and 5% in rectal cancer than the most affluent group.

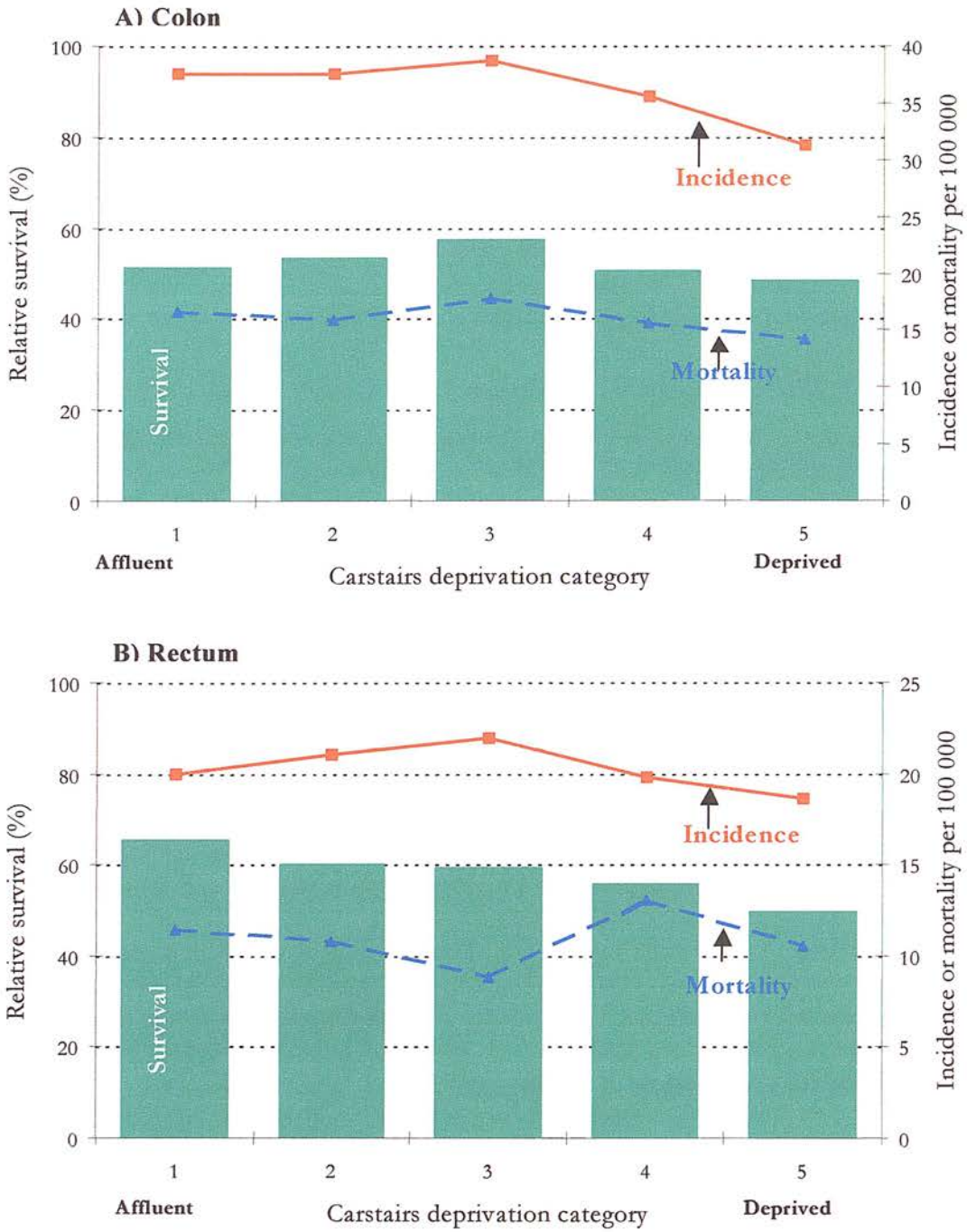
The survival rate gap increased between the most affluent and the most deprived groups for those diagnosed in 1996-99 in both sexes. The colon cancer survival rate difference was 6% in males and 7% in females; for rectal cancer the difference was 9% in males and 8% and in females (Rowan & Brewster 2004).

Scotland

In 1997, those registered with a diagnosis of colon cancer in the Scottish cancer registry showed a slight increase in the two-year survival for the most affluent group versus the most deprived group. For those registered with a diagnosis of rectal cancer in 1997 there was significantly higher survival in those from the most affluent group than the most deprived group. Figure 12 shows the incidence, survival and mortality of cases diagnosed with colorectal cancer in Scotland in 1997.

Hole & McArdle (2002) found that of those recorded as having curative surgery the most deprived group had a lower survival than the most affluent group. The more affluent individuals had a 68% five-year survival rate versus a 62% survival rate in the deprived group.

Figure 12 ***Colorectal cancer in Scotland: incidence (in 1997) and two-year relative survival rate and mortality rate (in 1999), by deprivation category and site of cancer***



(reproduced with permission from ISD 2003)

Studies investigating deprivation and colorectal cancer measured survival as the main outcome. Survival is viewed as the best possible outcome and is often used as an

indicator of effective cancer care. Survival is measured as the period between diagnosis and death (Dickman et al 1997).

In addition to differing socioeconomic status measures and different populations studied, the analysis of the data and the presentation of results are inconsistent. There are a variety of analytical methodologies used and therefore results are presented differently. Table 13 shows analysis methods used by studies reporting on survival rates.

Table 13 Analysis methods used to present survival data

Author	Year	Analysis Methods
Kogevinas	1991	Median survival time
Brenner	1991	Relative Hazard of Death
Auvinen	1991	Relative survival rate
Monnet	1993	Raw Survival
Schrijver	1995	Relative survival rates
Desoubeaux	1997	Observed survival rates
Pollock and Vickers	1998	Standardise mortality rates
Ciccone	2000	Cox proportional hazards rate
Campbell	2000	Cox proportional hazards rate
Kim	2000	Cox proportional hazards rate
Polendak	2001	Cox proportional hazards rate
Hole and McArdle	2002	Overall survival and cause specific survival
Wrigley	2003	All cause and cause specific survival

Kogevinas et al (1991), Auvinen et al (1992), Monnet et al (1993), Schrijvers et al (1995), Desoubeaux et al (1997), Pollock & Vickers (1998), Ciccone et al (2000), all found that survival time was shorter in the more deprived groups. Polendack (2001) found that survival was greater in females than in males. Monnet et al (1993) noted a poorer survival rate in the most deprived group existed whatever the severity of the Dukes' tumour stage though the difference was most marked in the less advanced tumours. Auvinen et al

(1992) reported a 19% greater risk of death due to colorectal cancer for the lowest social class than the highest social class. Stockton (2001) found, using Scottish data, that there were no major differences between the deprivation groups in; age at diagnosis, sex, tumour stage or tumour grade at diagnosis. However, deprived patients had a higher proportion of metastatic tumours and worse comorbidity at diagnosis.

Socioeconomic status and health

Many researchers have investigated the socioeconomic hierarchy, which has been demonstrated to influence the incidence of myocardial infarction, stroke, diabetes, chronic bronchitis and many other longstanding health problems. Many researchers have identified that as household income decreases, illness and disability increases.

Socioeconomic status and cancer

Many publications exist in the area of inequalities in health and cancer. It is known that there are factors arising from an individual's lifestyle that increase the risk of developing certain cancers. Examples include cigarette smoking, excess alcohol intake and poor diet. These factors are more often found in the lower socioeconomic groups, and form part of the socioeconomic divide (la Vecchia et al 1992). In Scotland, for example, it has been shown that there is a higher incidence and mortality rate in cancers of lung, cervix and oesophagus in the lower socioeconomic groups.

In higher socioeconomic groups there is an increased incidence but no mortality difference in breast cancer and an increased incidence and lower mortality rate for colorectal cancer (ISD 2000).

Despite this higher incidence of breast and colorectal cancer reported in the more affluent socioeconomic groups (Coleman et al 2004), survival is greater than in the more deprived groups (Schrijvers et al 1995).

Proposed explanations for such socioeconomic differences include; differing urban and rural differences resulting in unequal access to quality health care (McLeod 1999, Campbell et al 2001), differences in treatment (Mc Leod 1999) and late presentation with symptoms (Dent et al 1983, Langenbach et al 2003, Flashman et al 2004).

Socioeconomic status and colorectal cancer

Worldwide literature is available on colorectal cancer and the effect of socioeconomic status. There is specific literature relating to socioeconomic status and incidence, mortality, survival, staging at diagnosis and treatment variations. There are major differences in the reporting of these studies therefore the interpretation of results should be with caution especially when applying results to a different population (Monnet et al 1993).

Socioeconomic status, tumour stage and colorectal cancer

There are conflicting findings within the literature on stage of tumour and deprivation, Brenner et al (1991), Monnet et al (1993), Mandelblatt et al (1996), Ionescu et al (1998), Ciccone et al (2000), Hole & McArdle (2002), all found that the more deprived presented with more advanced disease. No studies found the opposite, although some studies found that there was no association between deprivation groups and stage of tumour at presentation (Auvinen et al 1992, Pollock & Vickers 1997, Kee et al 1996, Brewster et al 2001).

Mandelblatt et al (1996) reported that those living in the lowest socioeconomic status areas were 45% more likely to be diagnosed at an advanced stage than those in the highest socioeconomic status areas. In two Scottish studies, Hole & McArdle (2002) and Ionescu et al (1998) published the distribution of tumour staging and reported the most noticeable difference in socioeconomic groups was in the early Dukes' staged tumours.

Hole & McArdle (2002) reported from a Greater Glasgow study that 6% of all the tumours were diagnosed at Dukes' stage A. Of all of the Dukes' stage A tumours, 7% of were in most affluent group and 4% in the most deprived group. Ionescu et al (1998), reported that 15% of their Tayside cohort were found to be at Dukes' stage A and 18% of these were found in the most affluent group and only 9% in the most deprived group. Tayside region is known to have a more affluent population than Greater Glasgow.

Socioeconomic status and treatment for colorectal cancer

Following Dukes' stage at diagnosis, treatment is the next principal determinant of cancer survival (Auvinen & Karjalainen 1997). In an attempt to find out why the more deprived group have poorer survival, researchers have hypothesised that differences in treatment may be the reason.

Emergency admissions

It has previously been shown that emergency admissions have a poorer survival rate than elective admissions to hospital most likely due to surgical complications, possible comorbidity and more advanced stage of disease. It has been reported that individuals with a lower socioeconomic status have a higher proportion of emergency admissions (Anderson et al 1992). Pollock & Vickers (1998) found that of those admitted as an

emergency, 34% were in the most affluent group and 56% in the most deprived group. Wrigley et al (2003) found only a weak association between emergency admission and socioeconomic status. Hole & McArdle (2002) reported from a population with high levels of deprivation that 32% presented with emergency admissions; they found no association between mode of admission and socioeconomic status.

Stockton (2001) found there was no difference in the deprivation groups for emergency admissions in 1997 in Scotland.

Curative surgery

There is some evidence in the literature that management of colorectal cancer differs in the more deprived group. Monnet et al (1993) used comfort[10] of housing as the measure of socioeconomic status and found that those in no comfort or medium comfort housing were less likely to received curative treatment. Desoubeaux et al (1997) found that differences in treatment were not significant in males but were in females.

There was no association between delay of treatment and social class but there was a difference in the numbers receiving surgical treatment (Auvinen et al 1992). In the highest social class 54% received surgery compared to only 44% in the lowest social class. The largest difference found was in the group with distant metastases, where 10% of those in the high social class received surgery versus 2% of those in the lowest social class.

10 No comfort housing - no indoor toilet or bathroom. Medium comfort housing - has toilet but no bathroom. Comfortable housing – toilet and bathroom

Access to treatment

Auvinen et al (1992) reported a shorter delay in the more affluent group after presenting with symptoms. However, there was no difference in delay of treatment within socioeconomic status groups, once diagnosis had been made.

Some studies have questioned the equality of access to treatment and the treatment provided to those in rural areas. Campbell et al (2001) reported little differences in those receiving surgery, chemotherapy or radiotherapy by socioeconomic status or by living in rural areas in Scotland. There was a trend towards a lower likelihood of receiving radiotherapy the further the person lived from a cancer centre. Auvinen et al (1992) reported social class differences in those who received chemotherapy and radiotherapy. Another Scottish study, (McLeod 1999) found that chemotherapy was less likely to be given to the most deprived group compared to the most affluent group.

Wrigley et al (2003) found that survival was not linked with socioeconomic status but was strongly associated with a specialist surgeon, concluding that access to a specialist surgeon is not a problem for the deprived.

Summary of socioeconomic status

Within the current literature most studies report that there is an increased incidence of colorectal cancer in the most affluent group, this would suggest that there is an association between socioeconomic status and colorectal cancer.

There is a consistent one and five year higher survival rate in rectal cancer than in colon cancer, through the UK. There are conflicting results published in the literature regarding an association with socioeconomic status and the Dukes' stage of tumour. The

majority of studies report that the most deprived group present with a more advanced stage of tumour than the most affluent group. The literature has some discussion regarding inequality and access to treatment resulting in a more advanced stage of tumour at diagnosis. However, there is little published evidence to suggest this is true.

Chapter 7

Comorbidity and Colorectal Cancer

Comorbidity

Comorbidity is the presence of one or more medical conditions at the time of diagnosis of subsequent disease. With an ageing population there is likely to be an increase in the absolute number of such conditions in the population. The existence of comorbid conditions and their treatment may influence a doctor's decision on further treatment or surgery.

Research has focused upon validity of the measurement tool used in a particular disease population and/or the usefulness of the measurement tool to measure outcome for the disease or diseases under study. Feinstein (1970) was first to report that the coexistence of various chronic illnesses had an important impact on the management and prognosis of cancer patients.

In the past 15 years, there has been a greater research interest in comorbidity and the impact on various outcomes, particularly mortality or quality of life. There is consensus in the literature that comorbidity is an increasingly important factor that all research studies concerned with outcome measurements, should attempt to collect (Ogle et al 2000, Mandelblatt et al 2001).

The following is an overview of comorbidity literature in the key areas of research.

Methods of collecting comorbidity data

There is considerable debate regarding the optimum measuring tool and optimum method of collecting comorbidity data. Currently, the most frequent method of data

collection is to use data extractors to access medical records (Yancik et al 1996, Newschaffer et al 1997, Schrivjers et al 1995, De Marco et al 1999, Coebergh et al 1999, Vaeth et al 2000, Gonzalez et al 2001).

Administrative databases are mainly used in large population studies and only a few countries have this resource available. Many data entry errors have been found when using administrative databases, compared with other methods of extracting comorbidity data (Newschaffer et al 1998, Extermann 2000, Humphries et al 2000).

Some studies use self-reported or personal interview to ascertain comorbidity (Silliman and Lash 1999, Fillenbaum et al 2000, Ogle et al 2000, Mandelblatt et al 2001). One study used a physician to record comorbidity information but the number of cases was relatively small (Munro and Bentley 2004).

Criticism of data extraction from medical notes has focused upon the accuracy of information extracted and the interpretation by extractors. Satariano and Ragland (1994), De Marco et al (1999) and Coebergh et al (1999), re-extracted comorbidity information from a sample of their own study populations and found 80-95% accuracy. Self-reported comorbidity is limited by the ability to recall by the participants. Silliman and Lash (1999) and Mandelblatt et al (2001) found women with breast cancer accurately provided information about their disease and related symptoms, this information correlated well with the information extracted from medical records.

One advantage of the interview or questionnaire methodology for self reported comorbidity is that it can be used in research studies where access to medical records is

not available through lack of staff or where financial resources prohibit other methodologies.

The option of a doctor collecting the comorbidity data has major resource implications for any research study and to date has been limited.

Measuring comorbidity

There are 13 different measures of comorbidity used in clinical research, recently reviewed by de Groot et al (2003). Four of the most commonly used indices in cancer research have been peer reviewed for validity and reliability in clinical research. The other nine measurement indices have not accrued sufficient data to assess their validity and reliability. The four most common indices are:

1. Charlson index - CCI (Charlson et al 1987a)
2. Index of coexistent disease - ICED (Greenfield et al 1987, Greenfield et al 1993)
3. Cumulative Illness Rating Scale - geriatric - CIRS G (Linn et al 1968, Miller et al 1992)
4. Kaplan (Kaplan and Feinstein 1974)

Many studies compare results from different indices on their study population (Mandelblatt et al 2001, Extermann et al 1998, Extermann 2000). The four most common will be discussed in more detail.

Charlson Comorbidity Index

The Charlson Comorbidity Index (CCI) was developed using data from a series of medial admissions to an urban teaching hospital and their one-year mortality rates. The

comorbid conditions used in this index were extracted from medical notes and subjected to a multivariate analysis, yielding a summary severity index of 19 chronic conditions. Each category has an associated weight of zero to six based on the adjusted risk of one-year mortality. The overall comorbidity score reflects the cumulative increased likelihood of one-year mortality; the higher the score the more severe the burden of comorbidity. This index also correlates with specific outcomes of postoperative complications, length of stay in hospital and discharge to nursing home (Deyo et al 1992).

The CCI index has been validated in studies that extract comorbidity information from medical notes using a pre-designed form with a list of conditions.

Index of coexistent disease

The Index of Coexistent Disease (ICED) estimates the severity of 14 comorbid conditions and provides an assessment of the functional disability caused by each. It is a significant predictor of functional status at 1 year. It includes two dimensions:

1. The severity of each of the 14 coexistent medical conditions- the Index of Disease Severity (ICED - DS)
2. The degree of physical impairment or overall functional severity caused by the comorbidity - the Index of Functional Severity (ICED - FS)

These two dimensions are combined to form four levels according to increasing severity of co-existent disease and functional severity. The final index is a global measure of comorbidity.

Cumulative Illness Rating Scale

The Cumulative Illness Rating Scale (CIRS) classifies 13 comorbid conditions by organ system and each condition is graded from zero (signifying no problems found) to four (severely incapacitating or life-threatening). This scale was slightly adapted by Miller et al (1992) for use on the elderly population who developed guidelines to enhance reliability, using the name CIRS-Geriatric or CIRS-G scale.

Kaplan Index

The Kaplan index uses two forms of classification; one is the type of comorbidity whether vascular or non-vascular and the second is the severity of the pathophysiology. This is rated on a four-point scale from zero (no comorbidity or easy to control) to three (recent exacerbation of a comorbid condition). The rating of the most severe comorbid condition is the overall comorbidity score.

Information extracted from medical records is unlikely to give any indicator as to the effect these comorbid conditions have on individual's quality of life, mobility or functionality. Therefore, the method of data collection and index used to measure comorbidity should reflect the outcome measures of each research study (de Groot et al 2003). Although these indices have been studied for many years, it appears that no one index will fit all purposes and possibly a combination of indices are required for some outcome measures (Mandelblatt et al 2001).

Comorbidity and treatment

Comorbidity is frequently reported in individuals aged over 65 (Balducci and Extermann, 2000). It is therefore not surprising that this is the target age group reported in the

comorbidity literature. The number and severity of comorbid conditions increases with age (Yancik et al 1998, Yancik et al 2001 (b)). Few comorbidity studies compare people with cancer under age 65 to those over 65 (Yancik et al 1998, De Marco et al 1999 and Coebergh et al 1999).

Eligibility criteria for most clinical oncology trials require prior good health in the trial population. Many individuals aged 65 and over are excluded from these trials and therefore the study findings cannot be generalised to this age group, in the cancer population. As comorbidity increases with age, a greater proportion of the cancer population will be excluded from oncology trials. Existing comorbidity may mean that individuals are not offered standard treatment for their cancer. Havlik et al (1994) and Newschaffer et al (1997) showed this in their studies of women with breast cancer, as did Smith et al (1995) in a lung cancer study. Schag et al (1994) found that patients with prior comorbidity and lung and prostate cancer were less likely to be offered surgery.

There are some appropriate reasons for deviation from standard treatment. The toxicity of treatment may be harmful with certain chronic conditions or may affect independent living. In a recent study, Extermann and Balducci (2003) found that older cancer patients tolerate chemotherapy, even though they may experience some degree of toxicity. It had little impact on their independence, their comorbid condition or their quality of life.

It has been argued that the true effect of treatment in a range of comorbid conditions will not be known unless more individuals with comorbidity are offered entry into trials or given standard treatments and surgery (Extermann 2000, Gijsen et al 2001, Yancik et al 2001 (a)). Mandelblatt et al (2001) noted in her cohort of women with breast cancer

that the life expectancy, even for the more sick patients, was eight years and stated fears that older patients with comorbidity are being under treated.

Comorbidity and outcome

Survival

The current literature is highly focused on the impact of comorbidity on survival. Charlson et al (1987) developed an index of 19 comorbid conditions weighted for their impact on mortality. Later, Charlson et al (1994) developed a combined age-comorbidity score. The Charlson index has become the most frequently used scale in measuring the impact of mortality in cancer studies (de Groot et al 2003). Virtually all research studies using the Charlson index found it to be a valid and reliable predictor of mortality.

The following researchers have used the Charlson index, for breast cancer studies (Charlson et al 1987, West et al 1996, Ballard-Bash et al 1996, Newschaffer et al 1997), prostate cancer (Zincke et al 1994), head and neck cancer (Singh et al 1999), colorectal cancer (Munro and Bentley 2004) and also a study with various cancers, which included many of the above (Gonzalez et al 2001).

The above studies addressed a variety of cancer sites but only a limited number have reported on survival in colorectal cancer patients. Gonzalez et al (2001) showed that following a diagnosis of colorectal cancer; survival was poorer for those patients with comorbid conditions, compared to those with no comorbidity. Munro and Bentley (2004) demonstrated that comorbidity has an important influence upon the overall survival and the cause specific survival in patients with colorectal cancer. Stockton (2001) found comorbidity was strongly correlated with survival rate. Future studies

reporting on survival rate in the future should therefore include a measure of comorbidity.

Functionality or Quality of life

Also of interest to researchers are the effects of comorbidity on functional status of people with cancer (Extermann et al 1998). It is felt that this should also be measured along with the number and severity of comorbid conditions. The Kaplan index, described in more detail above, measures both comorbidity and functionality.

However, there are other measures of functional status that can be used along with an independent comorbidity index. It has been shown that comorbidity measures appear to be statistically independent of performance status and functional scales (Extermann et al 1998). At present there appears to be an agreement that no one comorbidity index can cover all aspects of the effect of comorbidity.

Delay in diagnosis

It has been suggested that individuals with serious comorbidity are less likely to be informed of surveillance recommendations for cancer, as they have a more urgent conditions requiring the attention of the GP (Jaen et al 1994). Cooper et al (1997) in a study of GP referrals for colorectal surveillance found that both doctors and patients felt that cancer surveillance has less value when there are other competing causes of morbidity present.

There is little literature relating to comorbidity and the effect it has on an individual reporting new symptoms to their doctor. There is some suggestion from earlier literature

by Crawford and Cohen (1984) that comorbidity may mask early symptoms and lead to later diagnosis. Conversely, there is a theory that individuals with chronic comorbid conditions attend their GP more frequently and therefore may be more likely to be sent earlier for investigations, with a possibility of being diagnosed at an earlier stage of the disease. Satariano and Ragland (1994) and West et al (1996) found that in women with breast cancer there was a trend towards earlier diagnosis of women with increased comorbidity. Neither of these studies used multivariate analysis, thus limiting the interpretation of their findings.

Gonzalez et al (2001) conducted a study in colorectal cancer, prostate cancer, breast cancer and melanoma and hypothesised that patients with more comorbidity would be diagnosed at a later stage of the disease. This study had a large cohort in each cancer site (8,933 colorectal cancer cases).

Multivariate analysis found overall that, taking all cancer sites together, a patient with any comorbid condition was more likely to have cancer diagnosis at a later stage of disease. However, further analysis of individual cancer sites suggested that this is true only for prostate and breast cancer. It was not found in colorectal cancer or melanoma.

Porta (1996) incidentally found in a small Spanish sample of 110 individuals diagnosed with colorectal cancer, 20 with oesophageal cancer and 52 with stomach cancer that those with more comorbidity presented to their GP sooner than those with no current medical illness at diagnosis.

Comorbidity, socioeconomic status and colorectal cancer

The influence of comorbidity on survival has had little attention in colorectal cancer studies and even less in studies combining colorectal cancer, socioeconomic status and comorbidity.

Polendack et al (2001) and Wrigley et al (2003) found that those with comorbid conditions had poorer survival than those without. They suggest that this may be a reflection of the choice of treatment for those with higher comorbidity. They used different measures of comorbidity, Polendak using the Charlson comorbidity index, and Wrigley making a simple count of condition in the medical notes, as the measure of comorbidity.

Stockton (2001) reported that comorbidity did not explain the deprivation-specific gradient in risk of death whereas, Wrigley et al (2003) found comorbidity was only associated with all cause survival. There remains no clear reason to why there is poorer survival in colorectal cancer for more deprived individuals. It is certain that increasing age, Dukes' stage of tumour and receiving curative surgery all have a positive impact on survival, but these factors do not fully explain the differences between socioeconomic status groups.

It has been suggested that in the most deprived group tumour biology is more aggressive which may be the result of nutritional, immune or comorbidity status (Auvinen 1992).

Summary of comorbidity

The current literature remains highly focused upon comparing comorbidity data collection indices and the outcome measures of these indices. However the Charlson comorbidity index was developed in 1987 and remains in use today and is the most commonly used index in UK literature. A proportion of this comorbidity literature also reports on the methodology of data collection and demonstrates that the most frequent methodology is using trained data collectors to extract data from medical notes.

As comorbidity is known to be more common in the age group over 65 years there are few studies report on individuals below 65 years. A section of this literature deals with the concern that many research studies exclude individuals with comorbidity and in doing so exclude a large proportion of the group aged over 65. Therefore results from these studies cannot be generalised to those over age 65. The literature concludes that researchers should include cases with comorbidity in their cohort in order to understand comorbidity and the interaction with common cancer treatments.

Chapter 8

Lower Gastrointestinal Signs and Symptoms

Lower gastrointestinal signs and symptoms

This chapter reviews the published literature on lower gastrointestinal signs and symptoms. A large proportion of the literature relates to reporting rectal bleeding to a GP and in particular rectal bleeding in the community. This literature is included in this thesis as it is closely linked with a diagnosis of colorectal cancer.

Lower gastrointestinal symptoms that can prompt a visit to the General Practitioner (GP) are rectal bleeding, change in bowel habit, abdominal discomfort or abdominal pain. All of these symptoms are reported frequently in primary care, and the task for GPs is to decide if the presenting signs or symptoms suggest a diagnosis of colorectal cancer.

A very extensive literature exists on all aspects of lower gastrointestinal symptoms and colorectal cancer and is dominated by the following areas:

- Rectal bleeding
- Delay in presentation
- Stage at diagnosis
- Delay in diagnosis
- Delay and mortality

Recent research has focused upon the combination of symptoms in the development of guidelines. The current literature on signs, symptoms and their outcome has primarily been in publications from a group of researchers in UK.

Rectal bleeding

Rectal bleeding is a symptom associated with colorectal cancer. Many studies have reported that rectal bleeding occurs in a large percentage of the general population, on most occasions, it is self-limiting and the large majority of cases do not seek medical advice.

Rectal bleeding is also prevalent in other colorectal diseases such as, haemorrhoids (Goulston et al 1986, Korkis and McDougall, 1995) and irritable bowel syndrome (Jones and Lyeard, 1992). This can make it very difficult for GPs to distinguish between rectal bleeding from a potential colorectal cancer and from other causes. There is a very fine balance between missing a diagnosis of colorectal cancer and subjecting large numbers of people to complex investigations, which are not without risk. These investigations can be anxiety provoking and physically uncomfortable for their patients. There is an added danger of overloading an already stretched NHS system by investigating individuals with a low risk of colorectal cancer.

Rectal bleeding in general population

The prevalence of rectal bleeding is reported as being present in between 18 and 20% of those aged 20-80years in the UK, (Jones and Lyeard 1992, Crossland and Jones 1995, Thompson et al 2000) and present in 15.5% to 20% of the Australian population (Dent et al 1986, Byles et al 1992, Talley and Jones 1998).

Few studies report on whether this bleeding was seen for the first time in the previous year or whether it had happened on previous occasions. The prevalence of rectal bleeding seen in the previous year was reported at 8.8% (Ferraris et al 2004) and 19%

(Crossland and Jones 1995) in the UK population. In the Australian population, Byles et al (1992) found only 4.5% had bleeding in previous year.

Another important factor for consideration when assessing rectal bleeding is the age at which individuals present. Crossland and Jones (1995), Talley and Jones (1998) and Thompson et al (2000) all found that rectal bleeding appeared to be more common in adults that were younger than age 50.

Three population based studies in the UK reported that only a few individuals ever seek medical advice for rectal bleeding, the following results were found 18% (Farquharson and Heald 1994), 28% (Thompson et al 2000) and 41% (Crossland and Jones 1995) this was also true for those individuals who have a family history of colorectal cancer that would increase their risk and yet do not seek advice.

Crossland and Jones (1995) reported that 66% of those reporting rectal bleeding were under age 50; much lower figures of 14% were found in Australia; these cases were age 65 and under (Talley and Jones 1998).

Thompson et al (2000) reported a positive predictive value of 1 in 709 for colorectal cancer from those reporting rectal bleeding in the community. This figure is similar to 1 in 1000 that reported by Fijten et al (1993) who estimated that only 7 per 1000 with rectal bleeding ever consult a GP and of these 2 per 1000 are deemed to have clinically important bleeding.

Reasons for not seeking advice on rectal bleeding

The percentage of people seeking advice for rectal bleeding varies across studies, in differing populations. The reasons given for not seeking advice are: not perceiving symptom to be serious (Crossland and Jones 1995), certainty that the bleeding is from haemorrhoids (McAdam et al 1979, Byles et al 1992, Crossland and Jones 1995) and hope that it would clear up (Byles et al 1992).

Haemorrhoids have been reported to be the most common cause of rectal bleeding in the general population. Goulston et al (1986) reported that haemorrhoids were confirmed as the source of rectal bleeding in 73% of the study sample, however, it was reported that 63% of those with haemorrhoids also had a concurrent colon lesion (not all colorectal cancer).

Rectal bleeding in those reporting to a GP Practice

Although rectal bleeding is common in the general population, few people ever report this to their GP; this has been referred to as the 'tip of the iceberg' (Thompson et al 2000). If everyone with rectal bleeding did attend his or her GP the system would be overloaded. Therefore, the public health message regarding rectal bleeding in the general population should be very specific and clear.

Individuals who do present to their GP with rectal bleeding are often eligible for research studies. This group of individuals is possibly an easier population to access for research purposes, as it provides the opportunity of follow-up to ascertain a diagnosis for the source of bleeding.

These studies vary in many important respects such as, the country of study population, sample size, ascertainment of the sample and age group included in sample. Not all studies specify whether rectal bleeding was an isolated symptom or if other gastrointestinal (GI) symptoms were also present in those diagnosed with colorectal cancer, thus making comparisons difficult.

Results from studies of rectal bleeding presenting to a GP and the results of follow up to diagnosis or discharge are shown in Table 14

Table 14 Percentage of individuals diagnosed with colorectal cancer after presenting to their GP with rectal bleeding.

Author and Year	Country	Sample size	Age	% diagnosed with colorectal cancer (number)
Goulston et al 1986	Australia	145	>40	10.3% (15)
Fijten et al 1995	Netherlands	269	18-75	3.3% (9)
Korkis & McDougall 1995	USA	102 -	<50	0%
Douek et al 1999	UK	91 with isolated bleeding 84 with rectal bleeding and other symptoms	All ages	2.2% (2) Rectal bleeding only 33.3% (28)
Norrelund & Norrelund 1996	Denmark	Study 1- 208 Same data collected 2 years later from different GPs Study 2 –209	>40	15.3% (32) 12% (22)
Dodds et al 1999	UK	8438	All ages	5.6% (471) 0.56% With rectal bleeding only
Wauters et al 2000	Belgium	386	All ages	7% (27)
Branagan et al 2004	UK	16,487	All ages	6.4% (690)

The most consistent reported result from studies interested in rectal bleeding is the prevalence of colorectal cancer. Most rectal bleeding studies accept those with rectal bleeding and other gastrointestinal symptoms in their inclusion criteria.

There were few studies that reported on rectal bleeding in isolation. Douek et al (1999) found that 20% presented with isolated rectal bleeding and 2.2% of these were diagnosed with colorectal cancer. Dodds et al (1999) found a prevalence of 0.56% for those with isolated rectal bleeding.

Studies reporting rectal bleeding and other associated symptoms, reported on the proportion found to have colorectal cancer. Goulston et al (1986) found 10.3%, Fijten et al (1995) reported 3.3%, Norrelund & Norrelund (1996) reported they found 15% and 10% in two cohorts in different time periods, in the one study, Wauters et al (2000) found 7.7% and Branagan et al (2004) reported 6.4% with colorectal cancer.

Rectal bleeding in isolation is not a good predictor of colorectal cancer and is common in the younger age group. The chance of a colorectal cancer diagnosis increases as a person makes their way through the NHS system. The lowest positive predictive value (PPV) is in those with rectal bleeding in the community, increasing in those presenting to GPs with rectal bleeding and the highest in those referred for investigations. Researchers have suggested that cumulative symptoms may be a more accurate guide to determine an individual's risk of colorectal cancer in the presence of rectal bleeding (Fijten et al 1995, Mant et al 1989, Norrelund & Norrelund 1996, Thompson et al 2000). This is supported by the recent research i.e. that a combination of symptoms may guide more appropriate referral for investigation (Thompson et al 2000, Selvachandran et al 2002)

Rectal bleeding and associated symptoms

There are several other symptoms that are associated with positive prediction of colorectal cancer. Norrelund & Norrelund (1996) found that age greater than 40 years and change in bowel habit are associated with an increased risk of colorectal cancer. Fijten et al (1995) reported that older age and palpable mass had an increased risk of colorectal cancer and Mant et al (1989) reported an association with dark red blood mixed with stool and absence of haemorrhoids.

Despite these findings by other researchers, Thompson et al (2000) cautions against the positive prediction of symptoms such as painless rectal bleeding, dark red bleeding and a change of bowel habit. They reported that these symptoms were all present in a high percentage of individuals in the community who also reported rectal bleeding to their GP and did not have colorectal cancer. They suggest that painless rectal bleeding without anal symptoms is a better indicator of colorectal cancer in this population.

Summary of rectal bleeding

Rectal bleeding is common in the community especially in the younger age group and in majority of cases it is self-limiting. Only a small proportion of those experiencing rectal bleeding ever seek medical advice for this symptom.

Differences in study methodology and reporting make the overall comparisons of these studies difficult. It appears that rectal bleeding alone is not a good predictor of colorectal cancer, although it was shown by Armstrong-James et al (1997) that those with rectal bleeding as the only symptom at diagnosis were more likely to have a Dukes' stage A tumour.

Delay in presenting with symptoms

Delay in presenting with GI symptoms remains a regular topic of publication. The literature presents the length of delay in various ways: delay from first symptom until presentation to a GP, delay from first symptom to diagnosis or delay from first symptom until surgery.

There are inconsistencies in data presentation within the literature on this sub-group.

1. Studies often give a breakdown on tumour site within the large bowel such as, rectal cancer and colon cancer. However, these are often inconsistent. Some studies report right-sided colon cancer and left sided colon cancer and may give no definition of where the right or left sided start and stop. Some studies report right sided and left sided as proximal and distal colon cancer. Some give the definition of the inclusions for these sites, which highlights these sub-sites vary between studies. Some studies include the sigmoid colon in the proximal colon and others do not. The definition of rectal cancer is sometimes cancer of the rectum only and, in other studies, rectal cancer includes the rectum and the recto-sigmoid junction.
2. When discussing delay it may be presented as mean delay or median delay, rarely both and with no reference to normality of distribution.
3. Timescale of delay differs through the literature and can be presented in days, weeks, months or in blocks of time such as >1month, > 3months or < 3months, without raw data this makes comparison very difficult.

Table 15 gives an illustration of the data presented in the literature for delay in presentation with gastrointestinal symptoms. Only studies reporting on delay until presentation at GP are included in this thesis.

Table 15 Reported delay time from first symptom until presentation to GP

Author	Year	Mean delay for Colon cancer	Mean delay for Rectal cancer	Sample Size
Shallow et al	1954	Site of colon dependent 35-42% waited < 6 months –	47% waited < 6 months –	750
Shallow et al	1954	Site of colon dependent 20-24% waited > 6 months -	31% waited > 6months –	
Holliday & Hardcastle	1979	12.7 weeks	16.2 weeks	200
McAdam	1979	Site of colon dependent 14 -22 weeks	17 weeks	150
Ratcliffe et al	1989	Site of colon dependent 60 – 62 days	90 days	332
Wheeler et al	1998	1979 – 12.7 weeks	16.2 weeks	100 colon 100 rectal cancers
Wheeler et al	1998	1995 – 9.6 weeks	20.8 weeks	
Armstrong-James et al	1997	Site of colon dependent 43 days	201days	224
Langbenbach et al	2003	93 days	157 days	70
		Mean delay for Colorectal Cancer		
Dixon et al	1990	Site of colon dependent 16 weeks-27 weeks	No breakdown given	202
Curless et al (b)	1994	Site of colon dependent 13-26 weeks		273
Porta	1996	25 days*		60 colon, 50 rectal 72, oesophagus & stomach
Roncorni et al	1999	10.8 weeks		100
Majumdar et al	1999	26 weeks		194
Gonzalez-Hermoso et al	2004	50% waited< 3 months 50% waited > 3 months		660

Site of colon dependent – information given for right and left sided of colon, however, some left sided include; the rectum and some rectal cancers include the sigmoid colon or recto-sigmoid junction.

*Median delay

Table 15 demonstrates the diversity of data presentation from studies concerned with delay with gastrointestinal symptoms. It is apparent from studies published over a period of 50 years, that there has been little change in the length of time people wait with

symptoms, before they present to their GP. Most studies report a mean delay of three months or more.

Wheeler et al (1999) collected data 16 years apart and found that the delay time for those with colon cancer improved and those with rectal cancer delayed almost twice as long as 16 years ago. The conclusion by the authors was that there is a lack of public knowledge associated with colorectal cancer. Table 15 presents information separately on colon and rectal cancer and provides evidence that those diagnosed with rectal cancer delay longer than those with colon cancer. The marked difference in time of delay is striking in some studies. In addition, it is reported that males delay longer in reporting symptoms (Hansen et al 1997, Potra et al 1996).

There was a variation in the methodology of data collection between studies although most studies collected data via interviews with the patients. Three studies used hospital records to collect their data (Shallow et al 1955, Majumdar et al 1999 and Gonzalez-Hermoso et al 2004). Data collection from medical notes has been criticised due to GPs selecting clinical data to write their referral letters and hospital doctors selectively recording information given to them by the patients.

Reasons for delay

Holliday & Hardcastle (1979), Porta (1995) and Wheeler et al (1998) asked individuals diagnosed with colorectal cancer why they waited a significant time before presenting to their GP. The results are presented in Table 16.

Table 16 ***Reasons given by colorectal cancer cases for not reporting symptoms promptly***

Reasons	Holliday & Hardcastle	Porta	Wheeler
Not concerned about symptoms	45%	44.3%	35%
Not serious enough to report	43%	23.5%	46%
Not serious disease or cancer	Not reported	88.5%	81%

Langenbach et al (2003) also asked the same question and his cohort responded differently, as follows; 50% 'feared unpleasant investigations', 40% hoped 'the symptoms would just resolve themselves with no need to report to a GP' and 10% had 'no reason at all for delaying to report symptoms'.

The reasons for delay in reporting symptoms that were given by those who had colorectal cancer are similar to the reasons given in a population-based study for not reporting rectal bleeding. Dent et al (1990) found that 13% with rectal bleeding assumed they had haemorrhoids, Byles et al (1992) found that 13% 'did not want unpleasant tests' and only 4% 'thought it could be cancer'. Kocher and Saunders (1999) found 27% thought 'not serious' and 27% 'hoped bleeding would stop'. The perceived seriousness of the symptom for that individual is the deciding factor, in reporting symptoms to their GP (Jones et al 1993).

Overview of studies reporting on symptom delay

Studies consistently reported a slightly higher number of males. On average the distribution is approximately 52% males to 48% females. This would match with registry data. The mean age range in these studies is 60-72 years. Most studies are in small populations, restricted to one hospital site. The majority of studies are from the UK with

a reasonable contribution from Australia, Netherlands and United States of America. The sample sizes vary from 44 to 750 recruits. Only a few studies focus on an age range, most have no age restriction.

Site distribution

The site distribution varies throughout the studies, most showing a slightly smaller proportion of rectal cancers. Shallow et al (1955) found the opposite with 63% rectal cancer and 37% colon cancers.

There are an increasing number of males diagnosed with rectal cancer (McSherry et al 1969, Bassett et al 1979, Ratcliffe et al 1989) and more females with right-sided colon cancer (Alley & McNee, 1986 and Stebbing and Nash 1995).

Alley & McNee (1986) reported a greater number of females in the >75 age group, but cautioned this may be because there are significantly more females, in this age group.

Dukes' stage distribution

Dukes' stage distribution is topical in many studies that report on delay in presentation. As the Dukes' staging definitions have been modified over time, there is a difference between the studies. The reporting of Dukes' stage of tumour will be dependent on the pathology department's criteria in use at time of study. Table 17 shows the distribution of Dukes' stage in published literature.

Table 17 Distribution of cases with colorectal cancer by Dukes' stage

Author	Year	Dukes' stage				
		A	B	C	D	Unknown
McSherry et al	1969	24.4	24.8	12.7		38.1
Bassett et al	1979	17	28	27.5		
Robinson et al	1986	5	49	28	18	
Stubbs & Long	1986	7	39	26	26	2
Ratcliffe et al	1989	8.7	48.1	27.4		5
Kyle et al	1991	10	42	23	25	
Anderson et al	1992	3	30	28	30	8
Curless (b)et al	1994 <70	9	33	25	31	
	>70	14	31	23	27	
Hansen et al	1997	12	43	43	2	
Roncorni et al	1999	17	30	39	14	
Young et al	2000	6	56	38		
Kiran & Glass	2002	A & B	53	C & D	47	

Diagnosis of Dukes' C tumours has increased in recent years and Dukes' D tumours were found in greater than 20% in many studies.

Curless et al (1994b) found that there was a trend towards the elderly not reporting symptoms and in particular change in bowel habit. However they found that those < 70 years had a higher percentage of Dukes' D tumours and those >70 year presented with more Dukes' A tumours.

Scott et al (2004) presented information from a single hospital in UK, over the period 1995 to 2003. Dukes' A tumours were reported at 18% in 1995 and to 9% in 2003 and Dukes' D tumours were reported at 24% in 1995 increasing to 32% by 2003; this increase was evident from the year 2000.

Dukes' stage and delay in presentation

The Dukes' stage of tumour at diagnosis will determine the outcome in terms of surgery, treatment and survival. Few studies investigating delay in presentation with symptoms found any correlation of any variable with Dukes stage at presentation.

Vineis et al (1993), Roncorni et al (1999) and Langenbach et al (2003) found a positive correlation between time delay in presentation and stage of tumour. Robinson et al (1986) reported a statistically significant correlation in rectal cancer only.

A more favourable Dukes' stage was found to be associated with longer presentation delay in some studies. Ratcliffe et al (1989) reported Dukes' B subjects delayed for 90 days and Dukes' C subjects delayed for 60 days. Similarly, Kyle et al (1991) found that of those who presented in under 12 weeks, 33% had Dukes' A versus 61.5% of those with Dukes' D. Wheeler et al (1999) and Bassett et al (1979) also found that the more advanced the tumour, the less delay. Wheeler et al (1999) reported that delay was greater in rectal cancer for Dukes' A and C tumours.

Although it is counterintuitive, Mulcahy & O'Donaghue (1997) reported that the longer the duration of symptoms, the more favourable the prognosis for recovery. There was a trend towards longer symptom duration in younger patients. The longest symptom duration was observed in rectal cancer patients, the shortest in patients with tumours of the left colon.

Family history

As family history is a known risk factor attempts were made to collect these data in some studies. In the majority of studies the definition of a positive family history was having one first degree relative with colorectal cancer. The following studies reported the prevalence of family history; McSherry et al (1969) found 5.1%, Ratcliffe et al (1989), 16% and Kiran and Glass (2002) 6.8% in their cohorts.

Ratcliffe et al (1989) and Kiran and Glass (2002) found a longer delay time of those with the knowledge of family history versus those not reporting knowledge of family history. In a study of reported rectal bleeding to GP (Mant et al 1989) 15 individuals were diagnosed with colorectal cancer and 10 had a family history.

Nichols et al (1999a) reported a weak association of family history and colorectal cancer in symptomatic patients. Family history was reported by 3.3% of those aged <65 and 11.8% of those >65. This is in contrast to other findings where hereditary colorectal cancer is more common in patients <65. This association may be stronger if guidelines are used as these have been found more accurate in identifying those at increased risk (Dunlop & Campbell 1997).

Other factors involved in delay

Other reported factors have been found to influence delay in reporting symptoms. Those who discussed their symptoms with family or friends were more likely to present sooner. The relationship to the person did not influence reporting and closeness of relationship was not found to be important (Holliday and Hardcastle 1979).

Dent et al (1983), Flashman et al (2004) and Langenbach et al (2003) reported that the more affluent had a shorter delay in presenting with symptoms. Langenbach et al (2003) also noted that those with private health insurance had least delay and those on welfare had the longest delay. Also those who were married reported symptoms sooner than those who were single, divorced or widowed. This supports the data published by Holliday and Hardcastle (1979).

Vines et al (1993) reported that advanced disease was commoner in those who were well educated, than those with fewer years of education.

Emergency admission

It is often assumed that those who present as emergency admissions have delayed in reporting symptoms to their GP and that the stage of disease is advanced.

The literature does not support an association between delay and advanced Dukes' stage. There is little statistically significant evidence that those presenting as an emergency have more advanced stage of tumours (Holliday & Hardcastle 1979 and Stebbing & Nash 1995). The advanced stage of tumour, together with the risks of emergency surgery, increases the risk of mortality. Table 18 identifies the percentage of individuals diagnosed with colorectal cancer that presented as an emergency within the various studies.

Table 18 ***Percentage of colorectal cancer patients with emergency admissions from published reports***

Author	Year	Admitted as emergency (%)	Comments
Holliday& Hardcastle	1979	42.0	76% had consulted GP concerning symptoms
Stubbs & Long	1986	26.0	Mean duration of symptoms 2.7months
Ratcliffe et al	1989	26.0	
Kyle et al	1991	23.0	20% had symptoms for longer than 1 month
Anderson et al	1992	36.0	
Curless et al (b)	1994	25.0	No difference in age
Stebbing & Nash	1995	33.0	
Mulachy & O'Donoghue	1997	**23.4**	2.7 emergencies for perforation 20.7 those presenting with obstruction
Roncorni et al	1999	18.0	
Wheeler et al	1999	**26.6**	1.5 Presented at A&E 25.1 acute presentations
Young et al	2000	15.0	
Kiran & Glass	2002	28.9	

The smaller percentage of emergency admissions found by Mulcahy and O'Donoghue (1997) and Wheeler et al (1999) are the number admitted via accident and emergency only. The higher percentage included those presenting with acute obstruction which is similar to the other studies. Interestingly, Anderson et al (1992) in a study of patients admitted to a Glasgow hospital reported that 36% presented as an emergency.

Emergency admission and Dukes' staging

There were a higher proportion of individuals with advanced Dukes' staged tumours admitted as an emergency, but this distribution was not significantly different from those admitted for elective surgery (Holliday & Hardcastle 1979 and Stebbing & Nash 1995). Anderson et al (1992) reported the proportion with tumours not staged was much greater in the emergency admissions (15% versus 6% in the elective admissions). Many

tumours have no stage because they are not removed, for a variety of reasons. Those admitted as an emergency and having no stage recorded at diagnosis are unlikely to be due to cancer within a polyp.

Emergency admission and delay in reporting symptoms

There is strong evidence that those who are admitted as emergency admissions do not delay longer than those with early stage disease. Stubbs & Long (1986) reported that mean duration of symptoms for the 55 (26%) admitted as emergency admissions, was 2.7 months but 40% of these individuals had symptoms for less than 2 weeks. Ratcliffe et al (1989) and Kyle et al (1991) also reported shorter symptom duration in cases admitted as an emergency admission.

Holliday & Hardcastle (1979) found that of the 42 (42%) cases admitted as emergency admissions, 76% had previously consulted their GP about symptoms. Of this 76%, 12% were currently under investigation at hospital outpatients.

Curless et al (1994 (b)) reported that cases >70 years were no more likely to present as emergencies than those <70 years. Anderson et al (1992) reported differently, with a higher proportion of age 75 and over admitted as an emergency. Emergency admissions are less likely to be rectal cancer, as noted by Anderson et al (1992).

Emergency admission and mortality

Anderson et al (1992) found that the 30-day mortality rate was significantly greater in emergency admissions and reported 28% mortality in emergency admissions versus 9%

in elective admissions. Stebbing and Nash (1995) confirmed this finding and reported 20.7% for emergency admissions and 3% for elective admissions.

Delay in referral for investigation

The issue of delay is commonly discussed in the literature and, in particular, there has been some debate regarding where in the process the longest delay existed, and where in the process the delay was most important in terms of affecting outcome. Not all studies report delay in presentation in a stepwise progression, some studies report an overall delay from onset of symptom until diagnosis or surgery.

McArthur & Smith (1984) and Curless et al (1994 (a)) have shown the delay by GPs to be the same as patient delay. All other studies found the patient delay to be greater than the medical delay. In one exception, Roncorni et al (1999) reported the mean patient delay to be 10.8 weeks with medical delay 19.5 weeks.

There is concern in the literature that simple procedures are not carried out on patients reporting gastrointestinal symptoms, citing:

- Abdominal and rectal examinations,
- Routine haemoglobin levels and proper investigations as to the source of anaemia,
- Proper attention paid to number and relation of presenting symptoms.

Abdominal and rectal examination

There is a high probability that colorectal cancer will be diagnosed if an abdominal or rectal mass is found during a physical examination. The palpation of an abdominal or

rectal mass should prompt a speedy referral for further investigations. However, the literature suggests that these routine examinations are not being carried out in the GP surgery.

McSherry et al (1968), McArthur & Smith (1984) and Langenbach et al (2003) reported only 29%, 32% and 23% of cases had abdominal examination at first visit to GP. McArthur & Smith (1984) noted that presentation with abdominal pain was the greatest prompt for GP to perform an abdominal examination.

McSherry et al (1968) reported 39% of rectal cancers were found by rectal examination, but did not indicate if this examination was carried out by the GP before referral. Bassett et al (1979), Holliday & Hardcastle (1979), Dixon et al (1990) and Wheeler et al (1999) reported that 90%, 77%, 70% and 78% of rectal cancers did have a rectal examination by GP before referral. Bassett et al (1979), Dixon et al (1990) and Wheeler et al (1999) found GPs correctly diagnosed a rectal cancer in a percentage of the cases examined, 53%, 47% and 50% respectively.

McArthur & Smith (1983) reported that only 34% of colorectal cancer patients were given a rectal examination on the first visit; this figure rose to 38 % after a second visit, a figure much lower than other studies. They also noted that when abdominal and/or rectal examinations were carried out there was a delay of no more than 3 days for referral. For those individuals not examined by a GP, 48% had not been referred after 3 months.

Dixon et al (1990) found that in individuals referred for treatment of haemorrhoids, 12% were found to have a palpable rectal cancer; however they had no examination by a GP. This alone resulted in delay of diagnosis. Wheeler et al (1999) found that in 22 patients who did not have a rectal examination by a GP 45% had a palpable tumour found at outpatient appointment. Results have shown that a high number of abdominal and rectal cancers were found by GPs when an examination was carried out. Adherence to protocols may prevent delays in referral to hospital.

Hennigan et al (1990) carried out a survey of GPs practice on rectal examinations and concluded that the reasons given for not carrying out a rectal examination on symptomatic patients were:

- Reluctance of patient
- Knowledge that the examination would be repeated again at outpatient department
- Lack of time
- No chaperone available

Iron Deficiency Anaemia

Iron deficiency anaemia is the most common cause of anaemia and affects approximately 1% of the population in the United Kingdom. The most common causes are bleeding from the gastrointestinal tract or uterus, and it can be a sign of underlying serious disease.

The quality of investigation and treatment for iron deficiency anaemia is questioned in the literature. Logan et al (2002) carried out a study in the community of individuals who were found to have iron deficiency anaemia. GPs were randomised to control or

intervention arms; the intervention arm received a prompt with prescribing details, follow up details and advice to investigate the cause. The results of this study improved appropriate prescribing but failed to impact on investigation. Of the individuals in this study, 7% were diagnosed with colorectal cancer within 12 months, 25% had no further tests and of these 40% did not have a normal haemoglobin level, within 12 months.

As has been previously reported, iron deficiency anaemia is present in a high percentage of individuals with right sided colon cancer. Ria et al (2004) investigated the role of iron deficiency anaemia as part of a surveillance programme. Haemoglobin estimations were carried out on all those under going flexible sigmoidoscopy. The aim was that left sided colon cancer would be identified by sigmoidoscopy and right sided colon cancer would be identified by iron deficiency anaemia. This study reviewed the 194 individuals with right sided colon cancer and iron deficiency anaemia, levels were set at <11g/dl in men and <10g/dl in females. Results showed that 44% of males and 57% of females had iron deficiency anaemia and concluded that iron deficiency anaemia alone is a poor predictor of right sided colon cancer.

Till and Grundman (1997) investigated the role of iron deficiency anaemia in the diagnosis of colorectal cancer, using a reference of <10g/dl for males and females. On reviewing notes 3 years later, 15% had a diagnosis of colorectal cancer. In a similar study, Stewart et al (2004) found 6.4% to have colorectal cancer, at time of initial investigations; no follow up period was reported. Archer et al (2003) studied the diagnostic delay in colorectal cancer within a group of individuals with iron deficiency anaemia. The study found that 38% of the cohort had iron deficiency anaemia at diagnosis, 12 % had this diagnosed for 6 months or more before diagnosis. There were significantly more right

sided colon cancers (65%) with iron deficiency anaemia, but no significance was found between iron deficiency anaemia and Dukes' stage of tumour.

The percentage of individuals with iron deficiency anaemia in colorectal cancer studies is given in table 19. In common with other inconsistencies in the colorectal cancer literature, the reporting of iron deficiency anaemia also varies between studies. Many studies do not publish the reference value used for anaemia, and, those who do, often use different base levels, possibly accounting for the wide range of results shown in Tables 19 to 23.

Haemoglobin levels are often extracted from medical notes, where it is recorded at time of diagnosis or surgery, while other studies record haemoglobin levels at time of referral from GP.

Shallow et al (1969), Alley & McNee (1986), Stebbing & Nash (1994) and Till & Grundman (1997) all found an excess of right sided colon cancer with iron deficiency anaemia. Goodman & Irvin (1993) report an excess of females, with right sided colon cancer. Also reported is that right sided colon cancers often present with iron deficiency anaemia a significant time before any other symptoms that are suggestive of colorectal cancer.

Goodman & Irvin (1993) and Roncorni et al (1999) both stated that the failure to investigate iron deficiency anaemia was the most common reason for GPs to delay referral and these people were more likely to have a delay of greater than 12 weeks.

Delay in referral and number of visits to GP prior to referral

The literature offers some insight into how many times a person visited the GP before referral to hospital for further investigation. Holliday & Hardcastle (1979), McArthur & Smith (1984), Jones et al (1993) and Wheeler et al (1999) reported 30%, 32%, 47% and 51.5% of patients respectively were referred to hospital, at the first visit. However, the same researchers found that a higher proportion of their study cohorts visited their GPs three or more times before referral to hospital.

These results have identified the difficulties that a GP encounters when he has a patient reporting symptoms that are common in the general population.

Number of symptoms at presentation

Little research has been carried out into importance of the total number of symptoms present at first visit to a GP. Two studies examining number of symptoms reported found at least three symptoms at first visit (McArthur & Smith 1984, Majumdar et al 1999).

Summary of delay

There is a wide representation of studies from UK, Europe and USA in the literature concerning delay in presentation with gastrointestinal symptoms. It is interesting that despite the different country of origin and likely culture differences, the delay time was consistently three months or more before presenting with symptoms and the vast majority of studies found an even greater delay. The length of patient delay has changed relatively little over the past 50 years, demonstrating that habits are difficult to change. In

contrast, in recent years, GPs have been referring more quickly, signifying an increase of knowledge and awareness of colorectal cancer symptoms.

The answer to the prolonged delay may lie in the fact that the mean age of the study cohorts are predominantly greater than 65 years and most studies report a higher proportion of males. It may be difficult for older individuals to discuss their toilet habits with their GP.

Delay in presenting with symptoms was found not to be associated with a more advanced Dukes' stage at diagnosis. Current guidelines emphasise the importance of early presentation to a GP and prompt referral for investigations. The benefits may be prevention of an emergency admission and the increased mortality that accompanies emergency surgery and prevention of increased anxiety if other symptoms develop. In addition, a symptomatic person's overall general health may deteriorate with prolonged delay in referral; this may complicate the postoperative period.

It has often been reported that individuals diagnosed with advanced disease have a short symptomatic period. However, a GP who manages his symptomatic patients expectantly may be blamed for delay, if cancer is later found.

Thompson (1999) reported that 14% of individuals may benefit from an earlier diagnosis of colorectal cancer and Armstrong-James et al (1999) felt that 28% would benefit as their tumour could have been diagnosed at a less advanced stage.

Reporting of symptoms

Many factors may influence when and why a person may report symptoms that are suggestive of colorectal cancer.

Symptoms reported by colorectal cancer patients

Several studies collected detailed information on symptoms reported. Similar to the other colorectal cancer literature, the results are published in a variety of formats. Results are presented for the whole cohort with colorectal cancer or for rectal and colon cancer separately. Others present results as right sided and left sided colon and rectal cancer or proximal and distal cancer. This lack of consistency adds to the difficulty in ascertaining a combination of symptoms, which may assist as predictors for colorectal cancer.

Symptom combinations indicating a possible site of colorectal cancer may also assist in the most appropriate first line surveillance method, for that patient. The results of these studies are given in tables 21, 22 and 23.

In addition to the differences in the site of cancer within the colon, lack of detail on reported symptoms also gave cause for concern due to the lack of clarification reported in each study. The most common symptoms reported in these studies are, rectal bleeding, change in bowel habit, abdominal pain, weight loss, abdominal or rectal mass and anaemia.

Rectal bleeding is either seen or not seen. Some studies give more detail on the colour of bleeding and whether it is mixed with stool or on the stool. Details of rectal bleeding will be discussed later.

Change in bowel habit is recorded but the type of change is rarely defined by most studies, limiting comparability. Interestingly, the study published by McSherry et al (1969) did give a definition of change in bowel habit as constipation or diarrhoea, or a combination of both, the classic presentation accepted for colorectal cancer at that time. In recent studies the change in bowel habit that has created most interest, is a change to looser, more frequent stools (Department of Health 2000).

Abdominal pain is reported regularly by studies, with no definition of whether this is acute abdominal pain or abdominal discomfort. A few studies do give more details as to the position of the pain in the abdomen. Several studies report high numbers of individuals presenting with abdominal pain.

Weight loss is probably the easiest symptom to detect but the methodology is important to exclude weight loss related to diet reduction or dietary changes.

Abdominal or rectal mass is commonly reported by studies, but not all studies reporting colorectal cancer differentiated between whether the mass is in the abdomen or rectum.

Anaemia is reported frequently with a great degree of inconsistency in the baseline measurement. Even where the baseline is given, it can vary between studies and some do not make any differentiations of levels for males and females. After the publication of NHS guidelines 'referral for suspected cancer' (2000), recent studies have been consistent in using the guidance.

Excess tiredness is sometimes reported as a separate symptom, and other studies combine anaemia and symptoms suggestive of anaemia, together.

Wind and bloating are symptoms collected by some studies; again inconsistencies appear when they are reported as individual symptoms, whereas most studies report them together, as one figure.

Table 19 shows percentages of cases with symptoms present on first visit to GP and table 20 shows all of the symptoms reported at any time before diagnosis.

Table 19 Percentage of cases with a presenting symptom on visit to GP

Author	Rectal Bleeding	Change in bowel habit	Abdominal pain	Weight loss	Anaemia	Excessive tiredness	Mass
Basset et al 1979	51		58	39			
Kyle et al 1991	44	56	41	17	11	7	
Hansen et al 1997	64	75	43	36	50		14
Young et al 2000	36	16	26		20		
Kiran & Glass 2002	37	48	34	24	16		2

Table19 demonstrates that those diagnosed with colorectal cancer present with three common symptoms, rectal bleeding, change in bowel habit and abdominal pain.

Table 20 Percentage of patient with colorectal cancer who report specific symptoms at presentation

Author	Rectal bleeding	Change in bowel habit	Abdominal pain	Weight loss	Anaemia	Wind and bloating	Tiredness	Mass	Tenesmus
McSherry et al 1969	51	73	65	57	3	12		29	
Curless et al 1994 (a)	52	71	51	47		40	43		36
Hansen et al 1997	43	52	58					67	
Roncorni et al 1999	38	65	45	15	50				
Gonzalez et al 2004	47	19	17		7			0.6	1.6

Table 20 illustrates that there are two common symptoms that individuals commonly report before diagnosis; rectal bleeding and change in bowel habit. In addition, a high percentage of individuals report abdominal pain and weight loss.

Tables 21 and 22 represent the symptoms reported by individuals with colon cancer divided by left and right sided cancer and table 23 shows symptoms reported by individuals with rectal cancer.

Table 21 Percentage of patients with right sided colon cancer who report specific symptoms at presentation

Author	Rectal bleeding	Change in bowel habit	Nausea	Abdominal pain	Weight loss	Anaemia	Mucus	Excess Tiredness	abdominal Mass	Tenesmus
Shallow et al 1955	29	57	35	77	70	31	6	30	55	5.1
McAdam 1979	14	82	54	91	40			59		
Curless et al 1994 (a)	18	50	33	73	62		8	68		5
Stebbing and Nash1995		11		22	38	74			54	
Majumdar et al 1999	43	56			46	70		31		4

Table 22 Percentage of patients with left sided colon cancer who report specific symptoms at presentation

Author	Rectal bleeding	Change of bowel habit	Nausea	Abdominal pain	Weight loss	Anaemia	Mucus	Excess Tiredness	Abdominal Mass	Tenesmus
Shallow et al 1955	41	73	28	68	45	5	15.3	11	43	5
McAdam 1979	43	84	70	68	43			48		
Dixon et al 1990	59	74		44	12	4			2	14
Curless et al 1994 (a)	44	70	20	70	48		33	48		23
Majumdar et al 1999	70	88			34	47				12

In the following table 23 a breakdown of symptoms for rectal cancer is given, but these studies sometimes include the sigmoid colon or the recto-sigmoid junction.

Table 23 Percentage of patients with rectal cancer who report specific symptoms at presentation

Author	Rectal bleeding	Change in bowel habit	Abdominal pain	Weight Loss	Anaemia	Mucus	Excess Tiredness	Rectal Mass	Tenesmus
Shallow et al 1955	55	71	11	40	4.7	13	13	75	29
McSherry et al 1969									72
Basset et al 1979	76							53	
McAdam 1979	77	84	54	30			39		
McArthur & Smith1984	68		22			28			
Curless et al 1994 (a)	75	81	30	46		44	30		55
Langenbach 2003	56								

Site within colon and comparison of symptoms

When comparing the above symptoms with site of cancer, it must be remembered that there will be an overlap between rectal cancers and left sided cancers, due to the differences in division points in the colon and some left sided cancers in these studies include the rectum. The division point of right sided and left sided colon cancer was inconsistent in many of the studies.

Rectal bleeding

Rectal bleeding was a more common symptom in left sided colon cancer and rectal cancer. The range for left sided colon cancer is 71-84% and rectal cancer had a range of 53-77%. Right sided colon cancer had a much lower range of 14-29%.

Change in bowel habit

A significant proportion of individuals with left sided colon cancer and rectal cancer reported a change in bowel habit. The range is 57-88% for left sided colon cancer, 40-81% rectal cancer and 11-82% for right sided colon cancer. In right sided colon cancer,

11% and 82% are the two extremes. Most studies found a change in bowel habit in slightly more than 50% of their cohort.

Pain

Pain as a symptom cannot be compared between rectal cancer and colon cancer, as the studies did not specify the site of the pain especially in studies reporting rectal cancer. However, in comparison to right sided colon cancer, left sided had a much lower range of pain recorded.

Reporting of rectal bleeding, changes in bowel habit and pain are common to virtually all studies. The following symptoms are only reported in some studies. The more detailed reporting of symptoms reflects the aims of the research study.

Nausea

Nausea is a rare symptom in those who are diagnosed with rectal cancer. A range of 20-70% is reported for left sided colon cancer and 33-54% for right sided colon cancer. Only two studies reported nausea in rectal cancer at 4% and 10%.

Weight Loss

Similarly to nausea, weight loss is more common in ride right colon cancer. Studies reporting weight loss showed a range of 30-46% for rectal cancer, 12-48% for left sided colon cancer and 30-70% for right sided colon cancer.

Anaemia

Anaemia is rare in rectal cancer and more common in right sided colon cancer. Right sided had a range of 31-74%, left sided 5-47% and only one study reported anaemia for rectal cancer at 4.7%.

Excess tiredness

Tiredness is reported independent of anaemia by some studies, although excess tiredness can be the result of anaemia. However, consistent with the findings of anaemia, reports show a range of 13-39% for rectal cancer, 11-48% for left sided colon cancer and 30-68% for right sided colon cancer.

Tenesmus

Tenesmus is unlikely to be a symptom reported by cases with right sided colon cancer. Tenesmus is reported in rectal cancer studies with a range of 11-55%, 5-23% for left sided colon cancer and 5-8% for right sided colon cancer.

Wind and bloating

Rectal cancer cases are unlikely to report wind and bloating as a symptom (not shown in table) Wind and bloating figure are reported together, left sided colon cancer 20-32% and 29-42% for right-sided colon cancer. Rectal cancer was reported by one study at 14%.

Mucus

Those diagnosed with right sided colon cancer do not often give passing of mucus as a symptom. Passing mucus was reported 15-33% with colon cancer, 13-44% for rectal cancer and only 6-8% of right sided colon cancer.

Abdominal and rectal mass

The reporting of the site of a mass was very unclear in some studies. Rectal mass was reported in 53-72% of rectal cancer studies. Abdominal mass was reported as 2-43% for left sided colon cancer, 54-55% for right sided colon cancer. It is not possible to make

any assumptions about these results as it is unclear, from the literature whether the figures given were at the time of referral or after examination by a physician or surgeon.

Specific characteristics of symptoms

In recent years, researchers have attempted to identify more specific details of some symptoms or to create a combination of symptoms which may guide referral for investigation.

Rectal bleeding

The colour of rectal bleeding has been reported as a predictor for a diagnosis of colorectal cancer. Researchers investigated whether the bleeding was bright red or dark, if the blood was mixed with the stool or on the stool. Fijten et al (1995) found colour of bleeding was of little value in predicting colorectal cancer. Mant et al (1989), Ellis et al (1999b), Chave et al (2000) and Branagan et al (2004) found that presenting with dark red bleeding as opposed to bright red was a slightly higher predictor for colorectal cancer.

Change in bowel habit

The term, 'change in bowel habit' is used throughout the literature and is commonly cited as highly prevalent and an important symptom in the diagnosis of colorectal cancer. The most common oversight of authors in the literature is that they fail to give a definition of the change in bowel habit. Without this clear definition it is not possible to make comparisons. Some of the more recent literature has addressed change in bowel habit and investigated if any specific changes have a higher predictive value.

In a community study of those presenting with rectal bleeding, Ellis et al (1999b) reported that those with a change to increased frequency and/or looser stool had a higher probability of a colorectal cancer diagnosis; this is compared to those reporting a change to less frequent stools and/or harder stools. Chave et al (2000) also had the same results in a study of those referred to hospital for investigations.

Anal symptoms

Until recently, in studies from the UK, the presence or absence of anal symptoms was uncommonly reported in the literature. In 1989, Mant et al reported a negative association with anal protrusion and Fijten et al (1995) reported that anal pain, anal itch or prolapse were not significantly associated with colorectal cancer. More recently, reports by Ellis et al (1999a), Ellis et al (1999b), Chave et al (2000) and Branagan et al (2004) have shown if any anal symptoms are present, this is a low predictor for colorectal cancer. Nichols et al (1999b) found that the combination of rectal bleeding without anal symptoms had an 11% positive predictive value, painless rectal bleeding alone had a 5% positive predictive value.

Combination of symptoms

Mant et al (1989) was the first to attempt using combinations of symptoms to predict the probability of colorectal cancer diagnosis. It was concluded that the signs and symptoms did not satisfactorily aid the decision on whether to proceed to full colonic investigations.

Fijten et al (1995) developed a model to predict those who should proceed to colonic investigations and those who have a low probability of colorectal cancer. They concluded that age over 60, rectal bleeding with blood on stool or mixed with stool and

a change in bowel habit, had a higher probability of colorectal cancer diagnosis. This study had only nine cases with colorectal cancer.

Majumdar et al (1999) also developed a symptom combinations model to predict the site of the cancer within the colon. The symptoms given for proximal cancer are; anaemia and the presence of any one of anorexia, nausea, vomiting, abdominal pain or fatigue. Symptoms for distal cancer given are; rectal bleeding, altered stools and the presence of any one of diarrhoea, mucus, rectal pain or tenesmus. This model had a sensitivity of 93% and a specificity of 47%. Other models have been developed in UK studies have specific guidance on the type of bleeding and characteristics of change in bowel habit.

Dodds et al (1999), Ellis et al (1999a) and Ellis et al (1999b) and Thompson et al (2000) have concluded that a combination of dark red rectal bleeding and change of bowel habit, to looser more frequent stools, have a high predictive value in the diagnosis of colorectal cancer. In the following studies the rectal bleeding and change in bowel habit is as referenced above. Dodds et al (1999) reported in those referred to outpatients with rectal bleeding, that rectal bleeding and change in bowel habit together identified 54% of all cancers, with a predictive value of 1 in 8. Ellis et al (1999b) refined this further, noting that 84% of patients with rectal/sigmoid tumours presented with change in bowel habit some with and some without rectal bleeding, 89% had a change in bowel habit to increased frequency and/or looser stools. These research studies played a major role in the development of Government guidelines on referral for suspected cancer (NHS 2000) these guidelines state that those who are suspected of having cancer should not wait more than 2 weeks for a hospital appointment.

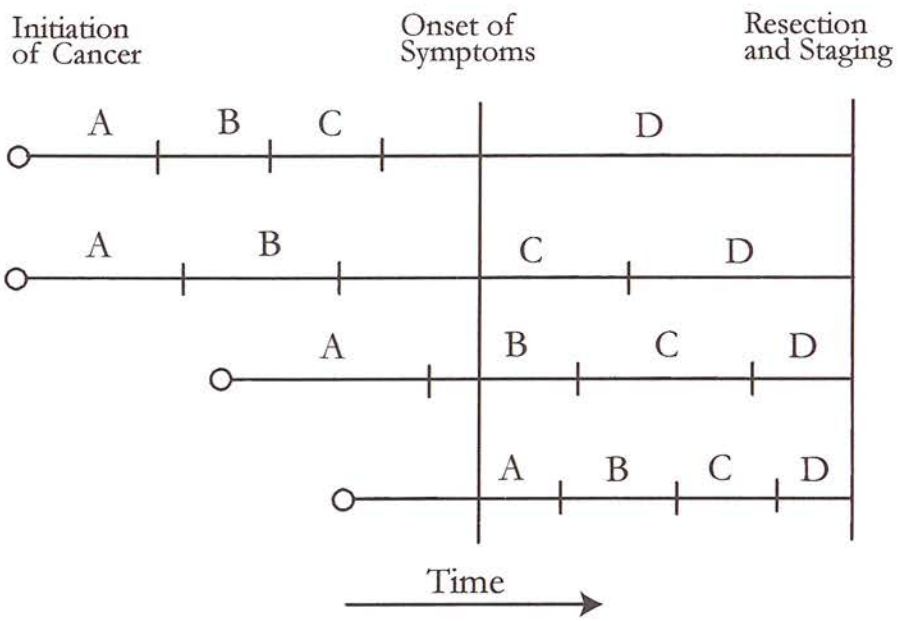
Selvachandran et al (2002) also used a combination of symptoms derived from the NHS guidelines and developed questionnaire and a computer based programme. Patients completed the questionnaire before endoscopy assessment, and data from the questionnaire and the referral letter, together were entered into the computer program. A weighted numerical score was derived from weighting of primary symptoms and symptom complexes, and was calculated automatically.

Using this program of a combination of symptoms than did not require Consultant input, it was found that there was no difference in cancer detection rate from the NHS guidelines (p=0 ·34), but that the NHS guidelines led to a higher rate of urgent referrals.

Pre-symptomatic colorectal cancer

In 1983 Dent et al published their theory on the progression of a colorectal adenocarcinoma through the Dukes' stages. Figure 13 illustrates that it is possible for a tumour to be at an advanced Dukes' stage before onset of symptoms. It is universally accepted that the more advanced the Dukes' stage at diagnosis, the poorer the prognosis and shorter survival time (Mulachy & O'Donoghue, 1997). This theory is now accepted and there is consensus that to improve overall survival from colorectal cancer the cancer should be identified before the onset of symptoms. In recent years the government has been addressing this.

Figure 13 Dukes' stage progression of an adenocarcinoma



Adapted from Dent et al (1983)

The Department of Health has provided funding for a pilot study of faecal occult blood testing (FOBT) in three sites within the UK. The aim is to identify colorectal cancer at an early Dukes' stage and remove a cancerous polyp or pre-cancerous polyps by colonoscopy, if possible. Some early tumours, Dukes' stage A, would require surgery but no chemotherapy minimising the physical cost of treatment for patients and the financial treatment costs to the health service. Those diagnosed at an early stage have a very high one-year and five-year survival rate (Mulachy & O'Donoghue, 1997).

Summary of reporting symptoms

There are some important indicators from the literature on lower gastrointestinal symptoms. A change in bowel habit is an important symptom in association with rectal bleeding. Many cases with right sided colon cancer may have iron deficiency anaemia for some time before the first gastrointestinal symptom is present and/or an abdominal mass is felt. Those with right sided colon cancer are more likely to present with pain.

Rectal cancers have a high probability of being found by rectal examination and individuals diagnosed with rectal cancer are more likely to have rectal bleeding and change in bowel habit but less likely to present with pain.

The complexities of lower gastrointestinal signs and symptoms suggest that, identifying symptoms that may be suspicious of colorectal cancer is a very difficult task for any GP.

Chapter 9

Development of Referral Guidelines for Suspected Colorectal Cancer

Referral guidelines

Guidelines were developed to assist GPs in the decision making process and unify care in the UK.

A committee derived from the Association of Coloproctology of Great Britain and Ireland, Royal College of General Practitioners and British Society of Gastroenterology, has reviewed published literature on signs, symptoms and outcomes. Following this review, 'The UK referral guidelines for Suspected Cancer' (Department of Health 2000) have been published. These were disseminated to all GPs in 2000. These guidelines are to assist GPs in deciding which patients are at high risk and which at lower risk, when presented with symptoms that are suggestive of colorectal cancer. They have not been designed to diagnose colorectal cancer in primary care.

The literature on lower gastrointestinal signs and symptoms in colorectal cancer, demonstrates the need for referral criteria in primary care. O'Riordan & Clifton (1999) carried out a study to produce criteria that would be sensitive and specific to significant colorectal disease, not only cancer. These criteria are as follows:

- Patients at 50 years of age or over with recent change in bowel habit;
- Any patient with recent change in bowel habit AND a strong family history of colorectal cancer
- Any patient with a carcinoma palpable on rectal examination.
- Patients with rectal bleeding AND another symptom.

In this study, all local GPs were sent the inclusion criteria and informed that all patients meeting the above criteria would be seen within one week of referral. The criteria were

deemed to be sensitive and specific to colorectal disease. Only 17% of new colorectal cancers diagnosed during the study period were identified by GPs using the criteria, despite the publicity given to this study.

Published referral guidelines

Colorectal cancer guidelines were published in a document called 'Improving outcomes in colorectal cancer' by the Department of Health (1997). This document has now been updated and published by the National Institute for Clinical Excellence (NICE) www.nice.org.uk (2004).

In response to a previous document 'The new NHS – Modern, Dependable.' Department of Health (1997) the NHS published a document 'referral guidelines for suspected cancer' (NHS 2000), which outlines the referral guidelines for several cancers. This document states that all patients meeting the criteria should be seen in clinic within two weeks, the 'two week wait standard'. It specifies high-risk criteria for colorectal cancer that would warrant an urgent referral to a fast track clinic.

Referral guidelines for suspected colorectal cancer in England and Wales

The guidelines shown in table 24 are divided into two levels; high-risk for fast track referral and a low risk for referral through the outpatient process.

Table 24 Referral guidelines for suspected colorectal cancer NHS 2000

Referral guidelines criteria for suspected colorectal cancer	Age Threshold
Rectal bleeding WITH a change in bowel habit to looser stools and/or increased frequency of defecation persistent for 6 weeks	*All ages*
A definite palpable right-sided abdominal mass	*All ages*
A definite palpable rectal (not pelvic) mass	*All ages*
Rectal bleeding persistently WITHOUT anal symptoms (* see below)	*Over 60 yrs*
Change in bowel habit to looser stools and/or increased frequency of defecation, WITHOUT rectal bleeding and persistent for six weeks	*Over 60 yrs*
Iron deficiency anaemia WITHOUT an obvious cause (Hb <11 g/dl in men or <10 g/dl in postmenopausal women)	

NB. Patients with the following symptoms and no abdominal or rectal mass are at very low risk of cancer:

- Rectal bleeding with anal symptoms*
- Change in bowel habit to decreased frequency of defaecation and harder stools.
- Abdominal pain without clear evidence of intestinal obstruction.

*Anal symptoms include soreness, discomfort, itching, lumps and prolapse, as well as pain.

These were the guidelines in use during the data collection of this study, however NICE plan to update these published guidelines, following a commitment in the NHS cancer plan.

NICE has commissioned the National Collaborating Centre for Primary Care to develop new referral guidelines for suspected cancer, to be used in the NHS of England and Wales. These are not expected to be available until mid 2005 (www.nice.org.uk). These

guidelines will incorporate any new published research and audit results since the publication of the previous guidelines.

Since the publication of the NHS suspected cancer guidelines that included the 'two week wait standard' for any individual suspected of having cancer, there have been many publications questioning (Sikora et al 2000, Willis 2000) and supporting their necessity (Summerton et al 2003). Audits carried out in the UK by Harinath et al (2002), Davies et al (2002) and Flashman et al (2004) confirm the validity of the high-risk guidelines for their diagnostic yield in colorectal cancer cases.

Harinath et al (2002) assessed 50 consecutive colorectal cancers and applied the high-risk criteria to them and found that 82% would have been eligible for fast track referral. Although the specificity was high, they felt that the sensitivity was too low for safety and recommended changes and a new addition to the criteria. They recommended changing the age threshold from 60 to 50. This would make the guidelines the same as the Scottish Executive guidelines.

They recommended adding abdominal pain with weight loss, even though using this is a criterion is very non-specific for colorectal cancer. Previous literature has shown these symptoms are found in high percentage of individuals diagnosed with colorectal cancer.

Flashman et al (2004) reported on effectiveness and efficiency of the referral guidelines for suspected cancers. It was found that 39% of referrals to the fast track clinic did not meet the criteria. They were disappointed that over 50% of those who did meet criteria were not referred to a two-week standard clinic. Of all colorectal cancer diagnosed in the

time of the study, 85% met the high-risk criteria. This study reported that there was no staging difference of Dukes' stage between those attending the two-week standard clinics and routine clinic.

Davis et al (2001) reported that 53% of colorectal cancers were diagnosed in the fast track clinic. Compared to 17% in the previous year when 48% of the colorectal cancer were diagnosed within two weeks. There was also a reduction in the number of emergency admissions from 40% to 30% for colorectal cancer.

A report from Soo et al (2001) reviewed case notes of 78 patients referred to one surgeon without using guidelines and applied the two-week rule guidelines to these cases. A significant benefit in terms of treatment times for colon cancer would have been experienced if the two-week guidelines were enforced. However for those with rectal cancer due to prolonged waiting time for staging and for pre-operative radiotherapy, there would be little benefit.

Moreea et al (2001) reported that the two-week waiting time standard was met but at the cost of a substantial increase in waiting time, an average of 30 days, for those attending the routine clinic.

Warwick et al (2004) reported that the two-week waiting time standard has changed clinical practice in their hospital. Before publication of the new guidelines, individuals were seen for a consultation, followed by investigations, if appropriate. This practice has been replaced with direct referral for flexible sigmoidoscopy and discharge on exclusion of colorectal cancer. These studies highlight the positives and the negatives of the new high-risk guidelines and the effect of two-week waiting time standard on clinical services.

Scottish referral guidelines for suspected colorectal cancer

The Scottish Intercollegiate Guideline Network (SIGN) published their first guidelines for management of colorectal cancer in 1997. Updated guidelines were published in March 2003. Within this publication are GP guidelines for referral. Before the updated version of the SIGN guidelines were published in 2003, the Scottish Executive Health Department (SEHD) published urgent referral guidelines 'Scottish referral guidelines for suspected cancer' in April 2002 for (www.show.scot.nhs.co.uk/sehd). These guidelines, shown in table 25, are similar to the 'referral guidelines for suspected cancer 'in the NHS 2000 document. Unlike the NHS guidelines for England and Wales, Scottish guidelines suggested urgent referrals should be referred to routine clinics labelled as urgent rather than utilising the specified two week model.

Table 25 Colorectal Cancer: Guidelines for Urgent Referral (SHED 2002)

Referral guidelines criteria for suspected colorectal cancer	Age Threshold
Rectal bleeding WITH a change in bowel habit to looser stools and/or increased frequency of defecation persistent for 6 weeks	*All ages*
A definite palpable right-sided abdominal mass.	*All ages*
A definite palpable rectal (not pelvic) mass	*All ages*
Rectal bleeding persistently WITHOUT anal symptoms (* see below)	*Over 50 yrs*
Change in bowel habit to looser stools and/or increased frequency of defecation, WITHOUT rectal bleeding and persistent for six weeks	*Over 60 yrs*
Iron deficiency anaemia WITHOUT an obvious cause (Hb <11 g/dl in men or <10 g/dl in postmenopausal women)	

NB. Patients with the following symptoms and no abdominal or rectal mass are at very low risk of cancer:

- Rectal bleeding with anal symptoms*
- Change in bowel habit to decreased frequency of defaecation and harder stools.
- Abdominal pain without clear evidence of intestinal obstruction.

**Anal symptoms include soreness, discomfort, itching, lumps and prolapse as well as pain.*

Scottish Intercollegiate Guidelines Network for colorectal cancer

Patients over the **age of 50 years** with any of the following symptoms over a period of six weeks should be urgently and appropriately investigated:

- Rectal bleeding with a change in bowel habit to looser stools and/or increased frequency
- Rectal bleeding without anal symptoms
- Palpable abdominal or rectal mass
- Intestinal obstruction
- All patients with Iron deficiency anaemia (Hb < 11 g/dl in men or < 10 g/dl in postmenopausal women) without overt cause should be thoroughly investigated for colorectal cancer.

Scottish GPs have access to both sets of Scottish of guidelines, which differ slightly in the age for referral; this may be confusing for GPs and any group who may be auditing the referral guidelines.

Implementation of clinical practice guidelines

Over the past decade, there has been an abundance of evidence based clinical practice guidelines produced for use in primary care. However, the current literature suggests that

GPs to do not implement guidelines readily. The continued proliferation of guidelines being produced requires the reasons behind poor implementation of guidelines to be understood.

Clinical practice guidelines have been defined as '*recommendations for patient management that identify one or more strategies for treatment*'. It is thought that as guidelines can be applied to all aspects of patient care such as; disease management, referrals, prescribing and preventative medicine, they can standardise and improve the quality of patient care (Grol 1992, Onion et al 1996). It is not possible for GPs to keep up to date with all the current research literature available for the many conditions seen in their daily practice. Therefore, it would appear that the simplest way forward for GPs would be to use evidence based guidelines.

Studies have attempted to understand the barriers to the implementation of clinical practice guidelines. In a qualitative study of GPs from several UK practices (Cranney et al 2001) found that the main barriers were shortage of time and pressure of work. Other reasons given were:

- Guidelines where developed on a motivated trial group of patients and not on the typical patient seen every day,
- GPs lacked ownership of the guidelines and therefore were not committed as not locally developed,
- Guidelines were not readily accessible.

Langley et al (2001) reported that GPs wanted local development and involvement with guidelines. Silagy et al (2002) found that when local guidelines were adapted from National guidelines they differed very little from the National guideline. This study used more than one method of introducing the guidelines to the groups and found that the

knowledge and practice had changed in both groups, suggesting that a multifaceted approach was important to effective implementation, rather than the changes to the actual guideline. This multifaceted approached was supported by Onion et al (1998) who also found that this use of multi educational approaches sustained the change in practice for at least 12 months.

It was also suggested that the guidelines need not be locally adapted but that locally known individuals working within the field of guideline to be implemented could be used in the dissemination process. This study reported that it is extremely costly to adapt National guidelines and the investment of time and money would be better utilised in the implementation process.

Other researchers have had similar results to the above studies and, in addition, found that to successfully implement guidelines, adequate support and time resources are required (Flottrop et al 2003), and as the most frequent reason for diversion from guidelines was patient pressure, the development of educational material for patients may help adherence to guidelines (Kerry et al 2000).

Despite the current issues surrounding the implementation and adherence to guidelines, they remain the way forward. With the introduction of clinical governance, a policy emphasising quality of care is required as a necessity to standardise many areas of patient care. Therefore, further research is required to optimise the implementation and use of guidelines.

There is little published information on the uptake of guidelines. The literature concentrates on the barriers to implementation and methods of implementing guidelines. The SIGN guideline report on auditing the implementation of the guidelines, predominantly in secondary care, reported that after implementing a local guideline, evaluation through re-audit was rare as was baseline audit (Millard 1998). Keaney and

Lorimer (1999) found minimal changes in the audit processes of implemented SIGN guidelines and concluded, that there was much work to be done, to embed clinical audit in the process of implementation.

In a UK randomised control trial of X-ray referrals in primary care, the intervention group were given updated, short and user friendly guidelines. When the guidelines were audited, a 20% reduction in referral for some x-rays was seen, compared to the standard arm.

There have been several audits on the referral guidelines for colorectal cancer, many reporting that high numbers of referral for 'two week rule' were inappropriate. Eccersley et al (2003) found that 45% of referrals did not comply with the guidelines and 38% non compliance was reported by Debnath et al (2002).

However, the audit of family history guidelines produced more positive results. Lucassen et al (2001) developed new guidelines using a local multidisciplinary team and disseminated these to GP practices. When audited, an improvement was seen in that 27% more referrals met guidelines.

There appears to be a message in this literature that the success of the guideline will be in the subject matter and the implementation process.

Knowledge of colorectal cancer symptoms, in the community

Guidelines can only be implemented if individuals with gastrointestinal symptoms present to their GP for assessment. There are small but significant number of individuals, who would benefit from an early presentation of their colorectal cancer.

Research into public awareness of the signs and symptoms of colorectal cancer has been published. Yardley et al (2000) carried out a telephone survey of the public and found

that only 31% were able to correctly state a symptom of colorectal cancer. Those most likely to know this information were older, female and from a higher social class. Those most unlikely to know a symptom of colorectal cancer were males under 25, of lower socioeconomic status.

Pullybank et al (2002) conducted a study of individuals attending a one-stop breast or rectal bleeding clinic. Each group were asked information on both breast and colorectal cancer, 47% of females were able to name a symptom of colorectal cancer against 27% of males; this was not statistically significant. Of these, 44% attending the breast clinic could state a symptom of colorectal cancer and only 37% of those attending the colorectal clinic could state a symptom of colorectal cancer.

Hughes et al (2004) circulated a questionnaire to those aged 50-80. Returned questionnaires were analysed for significant symptoms and subjects offered further assessment, if appropriate. To promote this study, a campaign was implemented to promote an awareness of colorectal symptoms. The 84.4% response rate reported was much greater than expected for a study of this methodology. The prevalence of symptoms in this study was 43.9%. Despite public health campaigns for colorectal cancer, the knowledge of the general population appears not to have improved dramatically. The study by Hughes et al (2004) has identified that small targeted health promotions can be successful without overloading the health system.

Chapter 10

Aims of the study

Background

Funding had been awarded by the Medical Research Council (MRC) for a very large collection of DNA and environmental exposure data from colorectal cancer cases in Scotland. The study for this thesis was undertaken within this DNA sample collection. The DNA samples were collected from individuals with colorectal cancer, age 16-79, diagnosed after September 2001 and normally resident in Scotland. This MRC study is known as the Study Of Colorectal Cancer in Scotland (SOCCS).

This prospective cohort study of individuals diagnosed with colorectal cancer gave the opportunity to record family history information from all recruited cases and to investigate the presentation patterns with lower gastrointestinal symptoms in relation to comorbidity and deprivation.

Literature

There is little literature reporting on family history pattern among a large series of cases with colorectal cancer. The current literature in this field concentrates primarily on the accuracy of the family history information given by the case against the information confirmed by cancer registry and medical records. This published literature lacks consistency in the definition of what constitutes a family history. The most common definition of a family history in this literature is *'one first degree relative with colorectal cancer'*. There are no published data investigating how a perceived family history of colorectal cancer influences; waiting time with symptoms, consideration of cancer before diagnosis, inspecting the toilet or toilet paper before flushing or the association with comorbidity or deprivation. There is little literature, particularly with a large cohort that report on the

proportion of cases with colorectal cancer and a high or moderate family history that is assessed using published clinical guidelines.

There is vast literature relating to delay in presenting with lower gastrointestinal symptoms but few published papers on the association with comorbidity and deprivation.

My professional interest in cancer genetics together with the lack of literature on colorectal cancer cases and family history (either perceived or assigned using guidelines) and the research opportunity afforded by the SOCCS study led to the following primary and secondary research questions.

Research questions

Primary questions

1. What proportion of individuals with a diagnosis of colorectal cancer perceived themselves to have a family history of colorectal cancer?
2. What proportions of individuals with a diagnosis of colorectal cancer are assessed to have an actual family history risk, (assigned using published guidelines)?
3. How does the number of cases with a perceived family history risk compare to those with an actual family history risk?
4. Does a perceived family history of colorectal cancer modify behaviour with respect to:
    - The knowledge of colorectal cancer symptoms?
    - The surveillance of toilet habits?

- Concern that lower gastrointestinal symptoms are symptoms of cancer before diagnosis?
- Shortened waiting time before presentation to GP with lower gastrointestinal symptoms?

5. Do GPs recognise family history as a risk factor in individuals diagnosed with colorectal cancer?

Secondary questions

1. Is waiting time with lower gastrointestinal symptoms among cases with colorectal cancer associated with:
   - Socioeconomic status?
   - Comorbidity?
   - Knowledge of colorectal cancer symptoms?
2. Do Scottish patients with colorectal cancer present with different symptoms or do they delay longer with lower gastrointestinal symptoms than other colorectal cancer population?

Aims

The primary and secondary aims of this thesis are:

Primary aims

- Ask information on family history and draw pedigree using only information given by the case, (no confirmations of cancers will be made).
- Ascertain and recruit the highest number of all cases, aged 16 -79, diagnosed with colorectal cancer and normally resident in Scotland, as possible, over 24 months.

- Report the number and proportion of cases that perceive they have a family history risk of colorectal cancer.
- Describe waiting time with symptoms and any behavioural differences in dealing with symptoms between those cases that perceive a family history risk and those not perceiving a family history risk.
- Report the number and proportion of cases in this cohort with a family history of colorectal cancer meeting Scottish clinical criteria for high or moderate family history risk.
- Report on the numbers referred to cancer genetic services and the numbers referred that meet Scottish clinical criteria for high or moderate family history risk.

Secondary aims

- Investigate any association between deprivation categories (using two deprivation indices) and the following:
    - Family history
    - Symptom presentation,
    - Waiting time with symptoms,
    - Comorbidity,
- Describe the symptom presentation and waiting time pattern of 1540 cases aged 16-79 diagnosed with colorectal cancer.
- Explore the role of comorbidity and delay in presentation of symptoms.
- Describe the percentage of the 1540 cases recruited that meet at least one referral criterion for suspected colorectal cancer.

Sample size

The projected sample size for this study was based upon pilot data gathered during the first three months of the SOCCS study. This recruitment approximated 50 cases per month. This study collected data for 24 months. A recruitment rate of 50 cases per month would give a total of 1200 cases. It was considered reasonable to assume that the recruitment figures would increase as the study became established and 25% was added to give a target total of 1500 cases.

Power

The pilot data for this study showed that 25% of cases perceived they had a family history of colorectal cancer and 18% of cases were assigned a high or moderate family history risk using published guidelines.

We based power calculations on the primary research questions that related to perceived family history, and those with an assigned high or moderate family history based on Scottish guidelines. In order to obtain estimates of the power to detect differences in proportions between groups, we considered 2 pairs of groups based on the above data from the pilot study.

These were those who were (n=270) or were not (n=1230) assigned a high or moderate family history risk and those who did (n=375) or did not (n=1125) perceive that they had a family history of colorectal cancer. Tables 26 and 27 below give each grouping and show the power to detect a significant ($p<0.05$) difference between the proportions in these pairs of groups for given true proportions. The results in the two tables are very

similar. These tables show that, for the above sample sizes and most comparisons there is a power of over 80% to detect a true difference in the proportions of 10% or more, and low power to detect smaller differences.

Since I considered this to be a difference which would be important to detect and was of a plausible magnitude, I concluded that the projected recruitment in the SOCCS study would permit a study of family history that would have sufficient power to be able to detect meaningful differences between the groups.

Table 26 Power calculations for those perceiving and not perceiving a family history

Proportion in second group (n=1125)	Proportion in first group (n=375)																		
	0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.5	0.55	0.6	0.65	0.7	0.75	0.8	0.85	0.9	0.95	0.99
0.1		0.722	0.997	1.000															
0.15	0.722		0.599	0.988	1.000														
0.2	0.997	0.599		0.520	0.973	1.000													
0.25	1.000	0.988	0.520		0.468	0.956	1.000	1.000											
0.3		1.000	0.973	0.468		0.433	0.941	0.999	1.000										
0.35			1.000	0.956	0.433		0.410	0.929	0.999	1.000									
0.4				1.000	0.941	0.410		0.396	0.922	0.999	1.000								
0.45					0.999	0.929	0.396		0.390	0.919	0.999	1.000							
0.5					1.000	0.999	0.922	0.390		0.390	0.922	0.999	1.000						
0.55						1.000	0.999	0.919	0.390		0.396	0.929	0.999	1.000					
0.6							1.000	0.999	0.922	0.396		0.410	0.941	1.000					
0.65								1.000	0.999	0.929	0.410		0.433	0.956	1.000				
0.7									1.000	0.999	0.941	0.433		0.468	0.973	1.000			
0.75										1.000	1.000	0.956	0.468		0.520	0.988	1.000		
0.8												1.000	0.973	0.520		0.599	0.997	1.000	
0.85													1.000	0.988	0.599		0.722	1.000	
0.9														1.000	0.997	0.722		0.898	1.000
0.95															1.000	1.000	0.898		0.988
0.99																	1.000	0.988	

Table 27 ***Power calculations for those assigned a high or moderate family history and those assigned a low risk family history***

Proportion in second group (n=1230)	Proportion in first group (n=270)																		
	0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.5	0.55	0.6	0.65	0.7	0.75	0.8	0.85	0.9	0.95	0.99
0.1		0.618	0.988	1.000															
0.15	0.618		0.501	0.963	1.000	1.000													
0.2	0.988	0.501		0.430	0.932	0.999	1.000												
0.25	1.000	0.963	0.430		0.385	0.903	0.998	1.000											
0.3		1.000	0.932	0.385		0.356	0.878	0.996	1.000										
0.35			0.999	0.903	0.356		0.336	0.861	0.995	1.000									
0.4			1.000	0.998	0.878	0.336		0.325	0.850	0.994	1.000								
0.45				1.000	0.996	0.861	0.325		0.319	0.846	0.994	1.000							
0.5					1.000	0.995	0.850	0.319		0.319	0.850	0.995	1.000						
0.55						1.000	0.994	0.846	0.319		0.325	0.861	0.996	1.000					
0.6							1.000	0.994	0.850	0.325		0.336	0.878	0.998	1.000				
0.65								1.000	0.995	0.861	0.336		0.356	0.903	0.999	1.000			
0.7									1.000	0.996	0.878	0.356		0.385	0.932	1.000			
0.75										1.000	0.998	0.903	0.385		0.430	0.963	1.000		
0.8											1.000	0.999	0.932	0.430		0.501	0.988	1.000	
0.85												1.000	1.000	0.963	0.501		0.618	0.999	1.000
0.9														1.000	0.988	0.618		0.817	1.000
0.95															1.000	0.999	0.817		0.962
0.99																1.000	1.000	0.962	

Chapter 11

Study Methodology

Eligibility for study

All cases aged between 16 and 79 years of age with colorectal cancer diagnosed after September 2001 and normally resident in Scotland were eligible for this study.

Exclusion criteria

Not eligible to be included in study

- Not normally resident in Scotland
- Squamous cell carcinoma of anus
- Melanoma of rectum
- Carcinoid tumours of colon
- Recurrent disease

Eligible - cannot give informed consent

- Too ill to give informed consent
- Mental health problems
- Learning difficulties
- Dementia

Ethical approval

MREC approval (approval number MREC/01/0/5) the local research ethics committee (LREC) approval was successfully obtained. Management approval was requested and gained from all Scottish Trusts.

Study development

Consultant consent

Consultant surgeons in all Scottish hospitals were asked permission for their eligible patients to receive information on the SOCCS study. Each consenting surgeon was offered an option for the author to visit them personally, or meet with the nursing staff involved in the care of their colorectal cancer patients. This visit would involve:

- Discussion and planning of how patients would be given the information packs,
- Discussion of the most appropriate way for SOCCS research nurses to liaise with the nursing team in that hospital.

Two surgeons in Scotland refused to allow their patients to be informed of the SOCCS study. One surgeon (who carried out emergency colorectal cancer surgery only) failed to respond after many reminders and the other was a colorectal surgeon.

Patients registered with either surgeon did not receive information on the SOCCS study and were recorded as non-participants.

During the course of this study, patients were identified with the diagnosis of a polyp cancer that did not require surgery. For these patients the Consultant Physician was sent a letter asking permission to offer their patients SOCCS study information and no refusals were received. It was the role of the research nurse to inform the SOCCS administration office of any consultant surgeons newly appointed within their hospitals of responsibility. New Consultants were then sent a letter, before any of their patients were offered information on SOCCS study.

All surgeons who perform surgery outwith the NHS were asked for consent to approach their private patients with study information and all agreed. When it was necessary to access information from audit and pathology departments, these department managers often requested a copy of the signed consent given by the Consultant surgeon.

Study awareness in hospitals

The most common method for dissemination of study information in hospitals was a presentation delivered by the author. This presentation was repeated several times to enable as many of the nursing and medical staff as possible to hear information on the study. Following this presentation a recruitment protocol was developed for each hospital.

In 23 hospitals that had a Colorectal Cancer Nurse Specialist, they became the main contact for the study, and a recruitment protocol was developed to suit their working practice.

Recruitment Protocols

Recruitment to the SOCCS study began in 36 NHS and Private funded Scottish hospitals, during September 2001. Each hospital had a recruitment strategy developed to ascertain eligible patients and provide them with the SOCCS information pack. In addition, a non-participant form was developed *(Appendix 8)* to record information on individuals eligible for the study, but unable for various reasons, to be offered the study information. The research nurses used this non-participant form to record individuals that had returned a reply slip indicating that they did not wish to take part. They also

recorded on this form those that did not reply within two months of having the information pack.

It is necessary to record minimum data to enable monitoring of ascertainment but it is deemed unethical to record identifying information on non-consenting individuals therefore the data recorded in this study for non-participants are:

- Sex
- Age at diagnosis
- Consultant
- Health Board where treated
- Reason for non-participation, if given
- Surgery – curative or palliative

Staff recruitment and training

The author developed the job descriptions for each post. Eight research nurses were initially appointed for eight geographical areas. Throughout the course of the study these geographical areas changed to meet the recruitment requirements.

The eight original research nurses attended a 3-day training session designed by the author. The principal investigators, project co-coordinator and the author delivered the training programme. All research nurses were given further one to one training with cases by the author.

During the first year of the SOCCS study research nurse meetings were held three monthly. Each meeting incorporated a session on the data collection specifically required for this study. These meetings were reduced to 4-6 monthly after the first year.

Case ascertainment and recruitment

Each research nurse activated the recruitment protocol initially agreed for the hospitals in their own area of responsibility. The initial plan for the SOCCS study was that the research nurse would visit patients in the last few days of their stay in hospital to recruit to the study if requested.

During development of the recruitment protocols, no members of nursing staff raised any objection to this proposal. Soon after recruitment commenced, a new discharge policy was implemented in most hospitals in Scotland. Colorectal cancer patients were discharged from hospital within 4-6 days of surgery in most cases, and this was not an appropriate time to recruit individuals to the study, as pathology reports had not been confirmed or the patient was distressed by their pathology result.

In many hospitals the research nurses met significant resistance from the nursing staff, as they were reluctant to inform patients of their eligibility for the study. Many nurses were unsure if the patients had been informed of their diagnosis. The study recruitment was least problematic in hospitals that had a colorectal cancer nurse specialist (CCNS).

These problems resulted in a change of recruitment protocols and cases were recruited in their own homes.

Data collection for this study

Family history data

If the case was willing to give family history information, a three-generation family history was taken at recruitment. The information was recorded on a family history sheet to assist with consistency of information collected *(Appendix 9)*. All research nurses had pedigree drawing training, using the universal nomenclature. Each family history was assigned a risk assessment using risk levels published in the Scottish Executive cancer genetic guidelines for colorectal cancer (Scottish Cancer Group 2001). The guidelines were chosen as they are used in all four Scottish Genetic Centres.

The following is the criteria for moderate and high risk:

Moderate risk:

- One first degree relative affected by colorectal cancer when aged <45 yrs;
- Two affected first degree relatives with one less than age 55 at diagnosis
- Three affected relatives with colorectal or endometrial cancer who are first degree relatives of each other and one a first degree relative of the Consultand

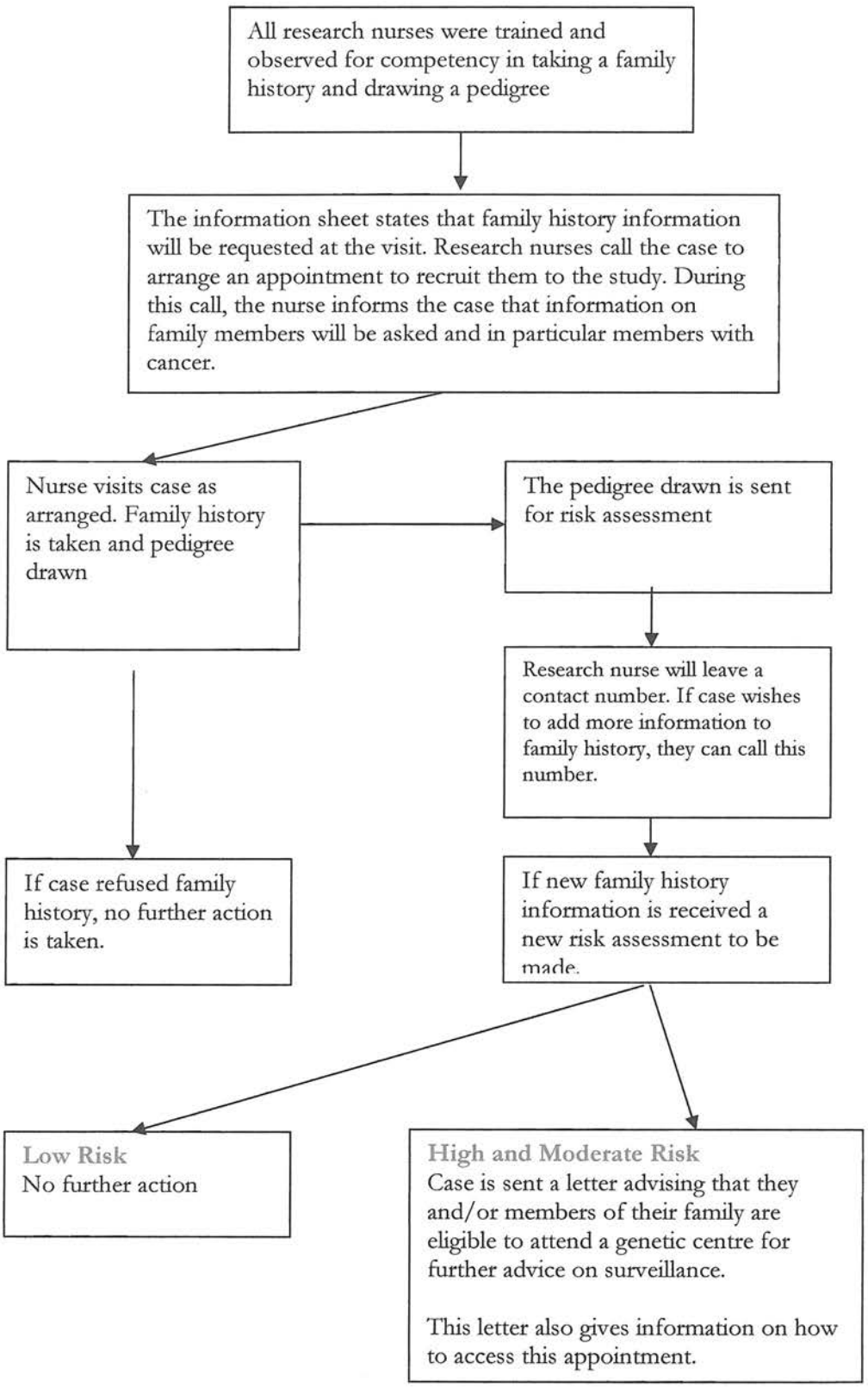
High risk:

- At least three family members affected by colorectal cancer or at least two with colorectal cancer and one with endometrial cancer in at least two generations; one affected relative must be age <or=50 at diagnosis, one of the relatives must be a first degree relative of the other two
- HNPCC gene carriers
- Untested first degree relatives of known gene carriers

Low risk:

- Anyone not fulfilling any of the above

Figure 14 *Procedure for obtaining a family history*



Risk assessment

Any person assigned a moderate or high-risk family history was sent a letter. This letter informed case of the risk assessment and included instructions on how they and relevant family members can access a cancer genetic clinic.

Genetic referral

High-risk cases are eligible for HNPCC mutation analysis testing and their first-degree relatives over age 30 (or five years younger than youngest affected relative) are eligible for surveillance by colonoscopy ever two years. In addition they are eligible for upper endoscopy every two years from age 50 (or five years younger than youngest stomach cancer if present in family history). Female relatives are eligible for discussion on ovarian and endometrial surveillance. Case would also be eligible for this surveillance after discharge from surgical follow-up.

Moderate risk cases are eligible for Microsatellite Stability Testing (MSI) of the tumour, their adult children and siblings over age 35 are eligible for asymptomatic colonoscopy surveillance at age 35 and, if normal, another colonoscopy at age 55.

Symptom data

An administered structured interview (*Appendix 10*) was the chosen methodology for symptoms data collection. The first draft of the symptom interview was piloted between March 2001 and June 2001. The first draft was mailed to known experts for comment. This process generated a number of interesting comments, and the second draft was developed to incorporate these.

The second draft was piloted on cases between September 2001 and December 2001 by the research nursing team. Amendments made for the final draft were based on comments from the research nurses about the layout, ordering of questions and the actual space provided for text. Throughout the study, the author personally recruited 5% of all recruits and supervised recruitments throughout the training process of each research nurse.

Question development

This structured interview comprised a combination of closed, semi-closed and open questions. A few questions have rating scales where appropriate. No appropriate existing measuring tool for the whole study could be found. However, communication with Mr. M Thompson, Consultant Colorectal Surgeon, during the draft phase of the questionnaire this resulted in sharing of information on a similar study of lower gastrointestinal symptoms on patients referred to a hospital outpatient clinic in the UK. The results of this study were not published at that time.

The questions from the data collection tool from Mr. Thompson were used for the development of Questions 4 and 5 'symptoms experienced prior to first visit to GP' It was intended that part of this study would replicate the work carried out by Mr Thompson's research team.

Other questions were designed using the Scottish Intercollegiate Guidelines (SIGN) for the management of colorectal cancer (1997).

Question 10 was added 'Looking at the contents of the toilet before flushing,' in response to several colorectal surgeons stressing to the author the importance of patients observing their own bowel movements.

Comorbidity data

This study collected comorbidity data using a recognised measurement tool. However, Professor D. Hole advised collecting information on hospital admissions in the previous two years would add further useful information on comorbidity. Therefore a question on previous two years hospital admissions was therefore added.

Family History data

The family history question was included due to the lack of literature in cases with colorectal cancer. This question was designed not to provoke anxiety during recruitment. Therefore the positioning of this question was important. During a visit to recruit a case it is more natural to ask about other aspects of their symptoms and care before discussing their family history risk as this may have biased their response to symptom questions. The final version of the symptom interview was ready for data collection in January 2002. The recruitment period for this study was 3rd January 2002 through to 31st December 2003.

It would have been good practice to re-administer a random sample of the symptom interviews for consistency and accuracy. However, the ethical approval for the SOCCS study did not allow re-contact with the subject after the initial contact visit.

Data entry

The symptom interview was designed using Teleform software version 7. The designed Teleform questionnaire enabled completed symptom interviews to be scanned and then read by the Teleform. Each completed symptom interview was scanned using a duplex scanner and imported into the Teleform package. All symptom interviews were checked for the quality of the ink markings before the scanning process. It is known that Teleform performs more accurately if the ink markings in boxes are firm through the centre of the box.

The symptom interviews were also checked for illegible handwriting that Teleform software would find difficult to read. This was made legible if possible, but most free text boxes were retyped at verification stage.

Teleform software verifies the data and verification can be set at different levels. Each symptom interview was verified using Teleform software and verification was set to stop at any unrecognisable letters or numbers in free text fields for each field. The verified data were exported into SPSS version 11.5, in preparation for data analysis. Once data were exported into an SPSS file, cleaning of these data were carried out by author.

Medical Record information

Specific consent was taken at recruitment to allow access to medical information stored in written or electronic form (*Appendix 11*). Information required by this study from medical records was included in a data collection form (*Appendix 12*).

All medical record managers in each hospital were contacted to discuss access to the medical notes of a recruited case. Each hospital had its own policy of allowing access to the medical records. Research nurses and medical students viewed the medical records that were available to them at each visit to medical records department. Each completed medical record form was checked for missing data before entry. The Charlson comorbidity index (CCI) (Charlson et al 1987) was incorporated into the medical records form (*Appendix 12*).

Data extraction from medical records

Each nurse or medical student involved in data extracting from medical notes was trained to extract this information by the author. Notes not available were re-requested each time a data extractor was attending that medical records department. For uniformity of collection they were asked to extract the data from the admission sheet, anaesthetic and surgical recording sheet, discharge letter and pathology reports.

For comorbidity data the CCI index sheet included a free text box for data extractors to write down any condition that was recorded in the notes but not on the list. They also had a comments box to write their own interpretation of anything they were unsure about.

It was not possible to record whether the conditions recorded were currently being treated. It was assumed if a doctor recorded a condition in the medical notes it was important enough to mention for ongoing management. The comorbidity index was checked for completeness before data entry. Data collection from medical records ceased on 31st July 2004. Many problems were experienced when accessing medical

records. Initially notes were requested three months after surgery to optimise the chance of availability. However, in year two this was changed to one month after surgery as it was found that even at three months, difficulty was experienced in getting access to medical notes. At one month it was possible the notes were in file awaiting first review appointment, which is normally at six week in many hospitals.

Comorbidity data

The Charlson comorbidity index is the most commonly used index in the literature. As the CCI index was developed for mortality outcome each condition is weighted. However, for this study the outcome measured was the total number of comorbid conditions prior to a diagnosis of colorectal cancer.

This study has used a simple count of CCI conditions named within the index. Two other conditions that were frequently noted in free text box were depression and alcohol abuse these have been included in the score of cases where recorded.

Deprivation data

Each person was allocated a deprivation scores derived from two independent deprivation indices, both allocated according to postcode at time of diagnosis. The indices chosen to measure socioeconomic status in this study are Carstairs deprivation index 2001 and Scottish Index of Multiple Deprivation 2003 (SIMD 2003).

Carstairs Deprivation index

Carstairs Deprivation index is categorised into 7 groups, 1 the most affluent and 7 the most deprived.

For this study, the scores have been condensed using methodology in common with other published literature. It is common in published literature using this index to have 5 groups or 3 groups, more commonly 3 groups are used. The 3 groups used in this study are condensed as follows:

- Group 1 = 1 & 2,
- Group 2 = 3, 4 & 5
- Group 3 = 6 & 7.

Scottish Index of Multiple Deprivation

The SIMD 2003 index is a new deprivation index and at time of writing there are no published papers. Therefore it has not been validated nor is there guidance on generating groups for least deprived to the most deprived unlike the Carstairs index. The statistician responsible for developing this index was contacted and asked advice on defining the groups using this studies data. However they could not advise. The scores in this index range from 1- 89; 1 is the most affluent and 89 is the most deprived.

The three groups defined in this study were assigned based on limited information in the report of the SIMD index. The report gave the top 100 most deprived regions and the scores ranged from 47.5 to 89. This range was used to define the most deprived group in this study. Groups 1 and 2 were derived from the equal divisions of the remaining scores into three groups; Group 1 is the most affluent and using the condensing principle applied in the Carstairs index. Groups 2 and 3 were condensed to define Group 2.

The SIMD group in this study are as follows:

- Group 1 = 0.00 to 8.66
- Group 2 = 8.67 to 47.49
- Group 3 = 47.50 to 89

All analyses carried out in relation to deprivation in this thesis report for both deprivation indices and are indicated in the text.

Three deprivation groups using Carstairs and SIMD deprivation categories are:

- Group 1 - least deprived,
- Group 2 - intermediate
- Group 3 - most deprived.

Pathology data

Only adenocarcinoma of the colon and rectum were included in the study, this information was confirmed from the pathology report. Information on Dukes' stage of disease, tumour, node and metastasis status were also gained from pathology reports, the minimum data set form or from a letter written in the medical notes.

Scottish pathology departments do not record the tumour staging information in a standard manner. Therefore, if elements of the staging data were not found, a request letter with patient consent was sent to the pathology department requesting the information required. Due to time constraints and problems accessing all medical records, this information was available for only 1212 of the 1540 cases.

Some individuals had no Dukes' staging was recorded for the following reasons:

1. A polypectomy was performed at colonoscopy and excision was complete
2. Surgery was not indicated due to other health problems
3. Palliative surgery performed tumour not excised for pathology
4. Radiotherapy was given before surgery and patient had a complete response and no residual tumour available for pathology.

Qualitative data

Almost all of the questions within the symptom interview had a free text box as a part of the question. After scanning and checking that all text fields had been read and the qualitative data interpreted properly by the Teleform reader, the data was taken into SPSS 11.5 for analysis. The author cleaned the data in each free text field and for each text field common categories were developed. This was then entered in to SPSS by recoding the data. The recoding of the data allowed this qualitative to be analysed using quantitative analysis methodology.

Chapter 12

Results: Ascertainment and Recruitment

Ascertainment

From 3rd January 2002 until 31st December 2003, a total of 3,761 individuals were identified with colorectal cancer, living in Scotland. Of this total 2,138 (57%) did not participate in the study. Of the total number not participating 856 are recorded as 'unable to take part'[11] and 1,223 cases recorded as 'did not want to take part'[12] in the study (reasons given table 29).

A further 33 cases gave no reason for not taking part and may have been in either 'unable to take part' or 'did not want to take part' group and a further 26 cases were patients of two non-consenting surgeons[13] that did not give consent for their patients to be approached. Further details of the ascertainment are shown in figure 15.
Table 28 shows a comparison of the two groups 'unable to take part' and 'did not want to take part' by sex, median age, surgery and their Health Board of residence at diagnosis.

11 Unable to take part'-eligible but decision made not to give study information

12 'Did not want to take part' not want to take part' – given study information and chose not to take part.

13 Non-consenting Surgeon – Surgeon not giving consent for his patients to be given the study information.

Figure 15 ***Ascertainment of eligible cases***

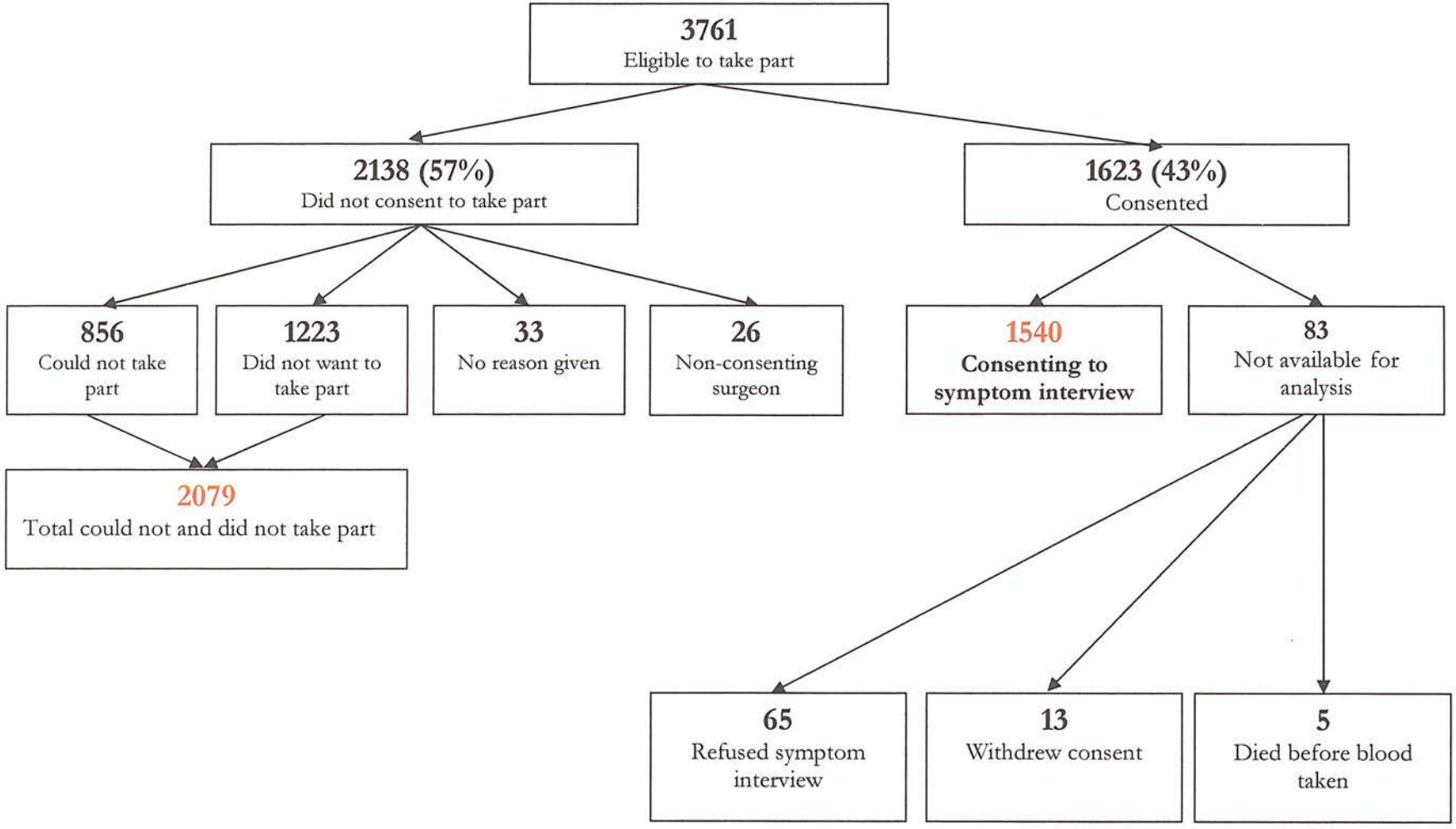


Table 28 Distribution of non-participants by Health Board of residence

	Did not want to take part		Unable to take part	
	1223	(%)	856	(%)
Males *	689	(56.5)	489	(57.1)
Females*	531	(43.5)	366	(42.8)
Median age**	69		70	
Inter-quartile range	63-74		63-76	
Surgery				
Yes	806	(65.9)	433	(50.6)
No	42	(3.4)	79	(9.2)
Unknown	375	(30.7)	344	(40.2)
Surgery Type				
Curative	394	(48.8)	70	(16.2)
Palliative	138	(17.1)	241	(55.6)
Surgery type not recorded	274	(33.9)	122	(28.2)
Health Board	**Total Number**	**% of all cases ascertained**	**Total Number**	**% of all cases ascertained**
Argyll and Clyde	90	(39.5)	50	(21.9)
Ayrshire	77	(30.3)	76	(29.9)
Borders	10	(13.9)	20	(27.8)
Dumfries & Galloway	50	(41.3)	24	(19.8)
Fife	76	(36.4)	36	(17.2)
Forth Valley	78	(39.0)	33	(16.5)
Grampian	132	(28.3)	67	(14.3)
Greater Glasgow	269	(38.0)	195	(27.6)
Highland	41	(28.7)	41	(28.7)
Lanarkshire	103	(30.5)	104	(30.8)
Lothian	168	(30.2)	147	(26.5)
Orkney	2	(22.2)	1	(11.0)
Shetland	7	(63.6)	1	(9.0)
Tayside	113	(38.6)	57	(19.4)
Western Isles	7	(50.0)	4	(28.8)

*For the group 'did not want to take part', the sex was missing for three cases and for those 'unable to take part' for one case.

** Age was missing for 15 cases that 'did not want to take part' and 12 cases that were 'unable to take part'.

Table 28 shows that in the 'unable to take part' group there was a greater proportion of cases that had undergone palliative surgery.

Unable to take part

There were 91(10.6%) individuals in this group that could not give informed consent, 31 had dementia, 47 had learning difficulties and 13 had mental health problems.

Table 29 lists the main reasons, if available, why a person was 'unable to take part' in the study. Those 'unable able to take part' were not given the study information to make the choice to take part.

Table 29 Reasons given by health professional why individuals were 'unable to take part'

Reason	856	(%)
Advanced Disease	204	(23.8)
Deceased	277	(32.3)
Dementia	31	(3.6)
Learning difficulties	47	(5.5)
Mental health problems	13	(1.5)
Unaware of diagnosis	11	(1.2)
Various other	86	(10.4)
No reason given by nurse	187	(21.8)

Table 29 shows that the two main reasons for cases 'unable to take part' are: the case died before receiving the information or the colorectal cancer nurse specialist made the decision that their disease was too advanced to give them the study information.

Of these 856 cases, 433 (50.6%) cases had surgery, 79 (9.2%) cases had no surgery was performed, 344 (40.2%) cases had no information available on surgical status. Of the 433 cases that had surgery, 70 (16.2%) of these had curative surgery, 241 (55.7%) had palliative surgery and for 122 (28.1%) the surgery type was unknown. Within the 79 cases where no surgery was performed, 41 (51.8%) were receiving palliative care and no

information was given why surgery was not performed for the remaining 38 (48.1%) cases.

When comparing these surgery data with the participants of the study, the surgery data were available for 1046 participants. Of these only 99 (9.5%) had received palliative surgery with the remaining 947 (90.5%) cases receiving curative surgery.

Did not want to take part

Of the 1223 cases that 'did not want to' take part the reason was not recorded for 1055 (86.2%) as the information was not given to the research nurse by the CCNS. For the remaining 168 (13.8%) the reasons given were:

- 56 (4.6%) were not interested,
- 28 (2.3%) had advanced disease,
- 2 (0.1%) died after getting information,
- 7 (0.6%) were too anxious
- 75 (6.1%) various reasons were given.

The source of the reason for a case not taking part was the CCNS or consultant surgeon and only in a small number of cases was the reason given directly by the case to the research nurse. Of all cases not participating in the study there was a statistically significant ($p<0.001$) difference within the proportions in each age group. In the age group 16-54 years 139 (6.7%), group 55-64 years 466 (22.4%) and in the group 65-80 1479 (71%) did not participate.

Participant

The total number of cases ascertained during the study period was 3761 and the number that initially consented to the study was 1623 (43%). Eighty three (5%) were not available for analysis as; 65 refused to answer the symptom interview, 13 withdrew their consent, 5 died before blood could be taken to complete recruitment. The final number of cases eligible for analysis is 1540 (41% of those ascertained).

For 328 (21.2%) of the 1540 cases, we were unable to obtain data from medical records, as they were not available in the medical records department at time of requesting. There was no difference amongst the cases with missing medical records in respect of, age, sex or deprivation groups using both deprivation indices. The exact number of cases available for analysis for each variable is indicated in the text where applicable.

Sex and age of participants

Amongst the 1540 cases there were 901 (58.5%) males and 639 (41.5%) females. The median age of participants is 65 years, the 25th centile is 57 years and 75th centile is 71 years. Table 30 shows the distribution of cases by age groups and sex.

Table 30 Distribution of recruited cases by age groups and sex

Cohort	Age Groups			Total
	16-54 years	55-64 years	65-80 years	
All	**309 (20.1%)**	**441 (28.6%)**	**790 (51.3%)**	**1540**
Males	162 (18%)	274 (30.4%)	465 (51.6%)	901 (100%)
Females	147 (23%)	167 (26.1%)	325 (50.9%)	639 (100%)

The distribution of participants by Health Board of residence at time of diagnosis is given in Table 31.

Table 31 Distribution of recruited cases by Health Board of residence

Health Board	Participating cases	% of all cases ascertained
Argyll and Clyde	88	38.6
Ayrshire	101	39.8
Borders	42	58.3
Dumfries & Galloway	47	38.8
Fife	97	46.4
Forth Valley	89	44.5
Grampian	267	57.2
Greater Glasgow	243	34.4
Highland	61	42.6
Lanarkshire	131	38.7
Lothian	239	43.1
Orkney	6	66.7
Shetland	3	27.3
Tayside	123	42.0
Western Isles	3	21.4

Table 31 shows that overall; Health Boards with large city hospitals have a higher proportion of cases participating in the study.

Table 32 ***Comparison of patients with colorectal cancer who were eligible for the study by consent status***

Gender & Age		Did not consent to take part		Consenting cases	
		2079	(%)	1540	(%)
Males		1178	56.8	901	58.5
Females		897	43.2	639	41.5
Median Age		70		65	
Interquartile range		63-75		57-71	
Surgery					
Yes		1239	59.6	1174	76.2
No		121	5.8	20	1.3
Unknown		719	34.6	346	22.5
Surgery Type					
Curative		460	37.1	941	80.1
Palliative		316	25.5	100	8.5
Not recorded		463	37.4	133	11.3
Health Board	**Total identified during study**				
Argyll and Clyde	**222**	140	61.4	88	38.6
Ayrshire	**254**	153	60.2	101	39.8
Borders	**72**	30	41.7	42	58.3
Dumfries & Galloway	**121**	74	61.2	47	38.8
Fife	**209**	112	53.6	97	46.4
Forth Valley	**200**	111	55.5	89	44.5
Grampian	**466**	199	42.7	267	57.3
Greater Glasgow	**707**	464	65.6	243	34.4
Highland	**143**	82	57.3	61	42.7
Lanarkshire	**338**	207	61.2	131	38.8
Lothian	**554**	315	56.9	239	43.1
Orkney	**9**	3	33.3	6	66.7
Shetland	**11**	8	72.7	3	27.3
Tayside	**293**	170	58.0	123	42.0
Western Isles	**14**	11	78.6	3	21.4

Table 32 represents a comparison of age, sex, surgery and the type of surgery performed and Health Board of residence for the total 2079 that did not consent to take part and 1540 that did consent to the study. This table demonstrates that cases not consenting to the study for any reason had more advanced disease than those consenting to the study.

Grampian Health Board had the highest number of consenting cases. This Health Board also had a low rate of 'unable to take part' and within that group a low rate of cases receiving palliative care.

Comparing those 'unable to take part' and those participating in the study, participants were more likely to have curative surgery than non-participants. The information on curative or palliative surgery was available for 1046 participants, of these 99 (9.5%) had palliative surgery and 947 (90.5%) had curative surgery.

There were 36 hospitals involved in this study, of these 21 had a colorectal cancer nurse specialist (CCNS) at start of the study, 4 hospitals appointed a colorectal cancer nurse specialist during the study and 11 hospitals had no CCNS. In the hospitals with a CCNS, the ascertainment of cases was over 75% of that expected. It was significantly less in hospitals without a CCNS. Although, it was noted that in 2 hospitals where there was no CCNS ascertainment was above 75%.

Recruitment by hospital

The following table 33 shows the percentage of the expected number of cases ascertained in each hospital. The expected numbers are based on ISD Cancer registry data for colorectal cancer diagnosed in 1999.

Table 33 ***Percentage of the expected numbers from 15 selected hospitals***

Hospital	Percentage ascertained of expected predicted number
1	134
2	75
3	68
4	91
5	98
6	62
7	83
8	69
9	72
10	110
11	75
12	84
13	45
14	77
15	72

Table 33 presents data from a sample of 15 hospitals to demonstrate the range of ascertainment. In all 36 hospitals, the ascertainment figures varied from 45% to 134% of the expected number.

Ancestry and ethnicity

Eligibility for this study required the case to be normally resident in Scotland; no specification was given that the case should be born in Scotland. It was of interest to know the percentage of cases that were born in Scotland and those with Scottish ancestry. On completion of this study, 1295 (84%) of the total 1540 cases had given information on ancestry and ethnicity.

1290 (99.6%) of cases reported themselves to be white Caucasian. The 1166 cases answered all of the ancestry questions and it was found that number of cases born in

Scotland and had parents or grandparents born outside of Scotland was relatively small. Figure 16 illustrates the number of cases that answered all of the ancestry questions and were born in Scotland. Of those born in Scotland, the number that had Scottish born parents and grandparents are shown.

It is important to note that the results of this study can only be generalised to populations of white Caucasians due to the very high percentage in this cohort and the extremely limited number of other ethnic groups.

Figure 16 *Number of cases, parents and grandparents, born in Scotland*

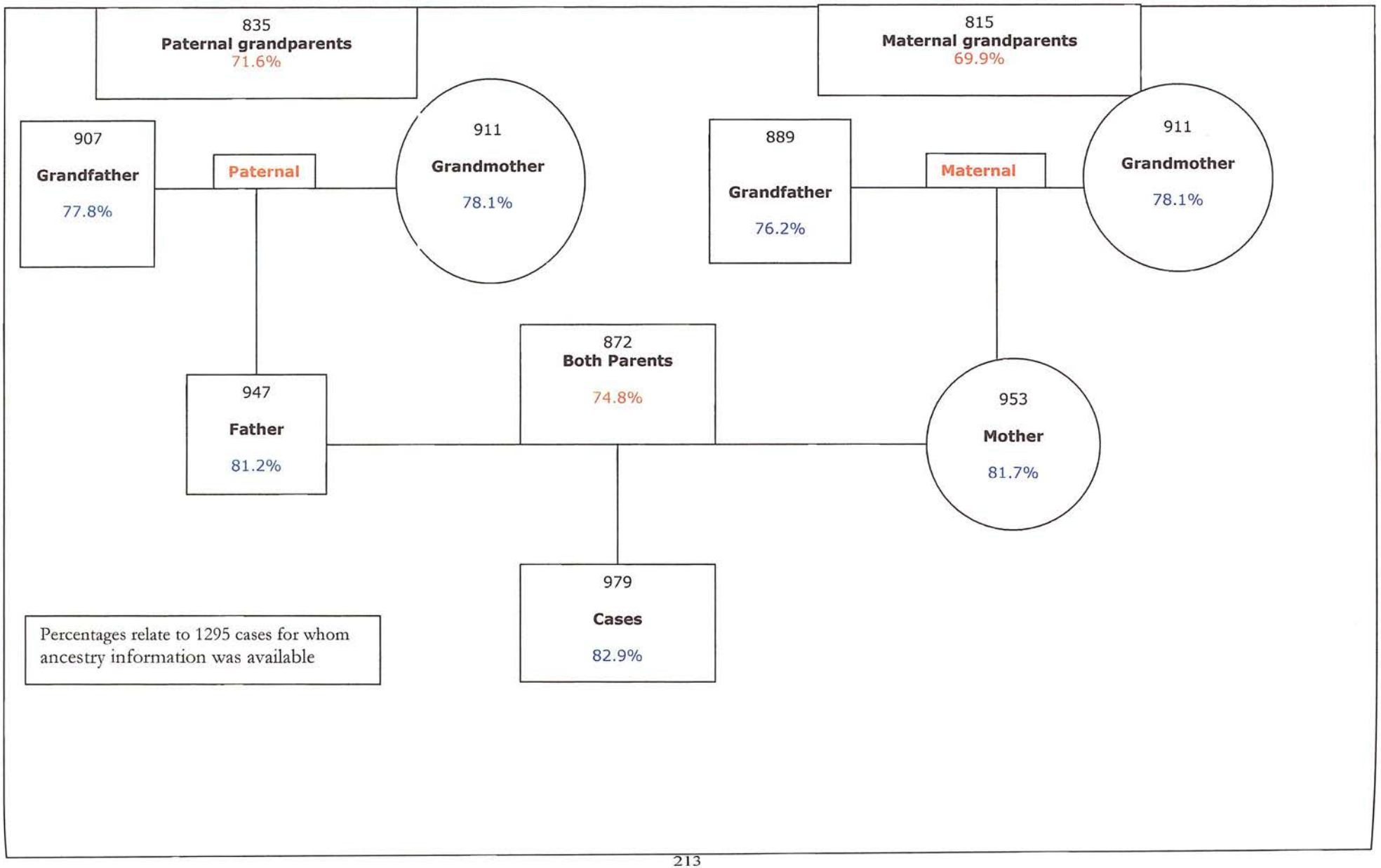


Figure 16 shows that 979 (82.9%) were born in Scotland and of those 872 (74.8%) had both parents born in Scotland. Of those cases with both Scottish parents, 815 (69.9%) had both maternal grandparents and 835 (71.6%) had both paternal grandparents born in Scotland.

The remaining 183 (14%) of these cases were born in other parts of UK and 39 (3%) outside of the UK. Those who answered 'other' to place of birth of their parents and/or grandparents ranged from 3% to 6%. Within this group there were a high proportion of parents and/or grandparents born in Ireland.

Distribution of deprivation scores

The Carstairs index and the SIMD index are the deprivation indices used in this thesis. Group 1 is most affluent; group 2 moderately affluent and group 3 is the most deprived. There was one Carstairs score missing for a case and two SIMD scores missing for two cases.

Table 34 shows the distribution of Carstairs scores and SIMD score for this study.

Table 34 Carstairs and SIMD deprivation scores for participants

Deprivation group	Carstairs score	2001 (%)	SIMD score	2003 (%)
1 (most affluent)	**417**	(27.1)	**470**	(30.6)
2	**912**	(59.2)	**942**	(61.2)
3 (most deprived)	**210**	(13.6)	**126**	(8.2)

Table 34 shows that there is some difference in the proportions within each group between the two indices

Table 35 compares the distribution of deprivation groups in the Scottish population for 2001 and the all reported cases of colorectal cancer diagnosed in Scotland during 2000 and this study population using Carstairs index. The Scottish data given in table 35 is from Information Services Division (ISD) of the Scottish Cancer registry.

Table 35 Carstairs deprivation score distribution for the Scottish population, cases register with colorectal cancer in Scotland and study population.

Carstairs score 2001	Scottish population (all ages) 2001	Scottish colorectal cancer population 2000 (16-79)	Study Population (16-79)
1 (most affluent)	25.8%	22.3%	27.1%
2	59%	62.8%	59.2%
3 (most deprived)	15.2%	14.9%	13.6%

Table 35 shows that the study population has a similar percentage of the most affluent and most deprived group as those registered with colorectal cancer in Scotland.

Comorbidity

The comorbidity score was derived from information given in the medical notes and reflects conditions present before the diagnosis of colorectal cancer. The Charlson comorbidity index was used with the addition of 2 conditions, depression and alcohol dependence. The scores are a total count with no weighting or measure of functionality[14]. The comorbidity score was available for 1208 cases.

The total scores range from 0 to 6, numbers and percentages are listed below in Table 36.

14 Some comorbidity scores have the ability to measure the effect of a comorbid disease on functional status.

Table 36 Comorbidity scores for 1208 cases by sex

Score	Total 1208	Score (%)		Males 719	(%)	Females 489	(%)
0	505	(41.8)		314	(43.7)	191	(39.0)
1	342	(28.3)		195	(27.1)	147	(30.0)
2	219	(18.1)		122	(16.9)	97	(19.8)
3	85	(7.0)		56	(7.8)	29	(5.9)
4	35	(2.9)		19	(2.6)	16	(3.2)
5	16	(1.3)		11	(1.5)	5	(1.0)
6	6	(0.5)		2	(0.2)	4	(0.8)

This table shows that 847 (70.1%) of cases had zero or one comorbid condition at time of diagnosis of colorectal cancer.

Further analysis of comorbidity scores was carried out using a variable code for those with no comorbidity and those with comorbidity. There was no statistically significant difference between male and females, age groups or deprivation groups (using both indices) in the proportions of those with or without comorbidity. Within each category with or without comorbidity the percentage of cases was higher in the older age group. Table 37 shows the results of this analysis for both deprivation indices and those with and without comorbidity at time of diagnosis.

Table 37 Deprivation groups and cases with and without comorbidity at diagnosis.

With comorbidity		Deprivation groups	No comorbidity	
Carstairs	SIMD		Carstairs	SIMD
193 (27.5%)	201 (28.7%)	1	145 (28.7%)	169 (33.5%)
407 (58.0%)	442 (63.1%)	2	298 (59.0%)	294 (58.2%)
102 (14.5%)	58 (8.3%)	3	62 (12.3%)	42 (8.3%)

There was no statistically significant difference between the groups with comorbidity or without comorbidity and the proportion in each Dukes' stage at diagnosis.

Type of admission to hospital

The medical notes were available for 1212 cases, 970 (80%) were elective admissions and 242 (20%) were emergency admissions.

There was no statistically significant difference in the proportion within the age groups, sex, deprivation groups or comorbidity of those admitted electively or as an emergency admission.

Cross tabulation of Carstairs index and type of admission to hospital was possible for 1185 cases and 1184 cases when using the SIMD index.

Analysis using the Carstairs index found no statistically significant difference in type of hospital admission between proportions in the deprivation categories. Although not statistically significant, there were a greater proportion of emergency admissions in the more deprived group. Emergency admission was recorded for 35 (25.2%) of the deprived group and 63 (17.8%) of the most affluent group.

Using the SIMD index, there was no statistically significant difference in type of hospital admission. Although not statistically significant, the emergency admission number was 20 (22.5%) in the most deprived group and was 77 (18.8%) in most affluent group.

Analysing the Dukes' stage and mode of admission to hospital there was a statistically significant difference ($p<0.001$) between those admitted as an elective admission or emergency admission and Dukes' stage of tumour. The results are shown in table 38.

Table 38 Dukes' stage of tumour and mode of admission to hospital

	Admission to hospital	
Dukes' stage	**Emergency (%)**	**Elective (%)**
A	20 (8.5)	225 (23.7)
B	91 (38.6)	348 (36.6)
C	105 (44.5)	327 (34.4)
D	16 (6.8)	29 (3.1)
N/A*	4 (1.7)	21 (2.2)

*N/A- no staging available as no surgery was performed

This table demonstrates that there is a large percentage difference in those presenting with Dukes' stage A tumours by mode of admission to hospital. There was a statistically significant difference ($p<0.001$) between proportions with colon cancer and rectal cancer and the mode of admission to hospital. In the group of cases admitted as an emergency 196 (82.7%) had colon cancer and 41 (17.3%) had rectal cancer.

Analysis of delay in presentation with symptom and mode of admission to hospitals is shown in table 39.

Table 39 Median delay time and mode of admission to hospital

Symptom	Median wait time (weeks)	
	Emergency	Elective
Change in bowel habit	8	12
Rectal bleeding	4	6
Weight loss	12	13
Marked loss of energy	13	13
Wind and bloating	8	13
Loss of appetite	8	13
Mucus	8	13
Tenesmus	12	13
Abdominal Discomfort	5	10
Pain	2	5.2
Nausea	2	8
Vomiting	1	1.5

Table 39 clearly demonstrates the shorter wait time with most symptoms in cases admitted as an emergency, with the exception of marked loss of energy, which has the same wait time as for elective admissions.

There was a statistically significant ($p<0.001$) difference between the proportions of cases with rectal and colon cancer and the mode of admission to hospital.
Of the cases admitted as an emergency 196 (82.7%) had colon cancer and only 41 (17.3%) had rectal cancer.

Chapter 13

Results: Family History

Family history

Of the 1540 colorectal cancer cases, 31 (2%) cases refused or were unable to give their family history for a variety of reasons. The main reason given was that the case was no longer in touch with their family. Therefore a total of 1509 cases were available for risk assessment. Of these, a total of 280 (18.6%) cases in this study were assigned a high or moderate family history risk, based on Scottish guidelines. The remaining 1229 (81.4%) cases were assigned a low family history risk. A proportion of cases assigned a low family history risk will have a close relative with colorectal cancer but they do not meet the specified guidelines. Throughout this section the family history risk assigned by the guidelines will be referred to as assigned family history risk.

The assigned family history risks are given in Table 40.

Table 40 Distribution of assigned family history risk using Scottish guidelines

Assigned family history risk	Frequency	%
High[15]	27	(1.8)
Moderate[16]	253	(16.8)
Low[17]	1229	(81.4)
Total	**1509**	**100**

Family History Data Analysis

The data in this section relate to questions 13 and 13b of the symptom interview (*Appendix 10*). Each case was asked 'would you say you have a family history of

15 High risk –families with three or more relatives with colorectal cancer over two generations who are 1st degree relatives to each other and one under age 50 at diagnosis.

16 Moderate risk –families who have a case under age 45 and are a 1st degree relative or two cases with one under 55 or three cases with colorectal cancer.

17 Low risk – families not meeting high or moderate risk

colorectal cancer?' The term 'family history' was chosen for the question, as it is the terminology used in health insurance documentation, it is also used by hospital doctors and General Practitioners (GP). By adulthood, most people have had some experience of GPs or hospital doctors or insurance documentation asking them about their family's medical history. Therefore, the term family history, in the above context, is understood by the general public to mean other people in their family with the condition of reference. No reference to risk was used or choice of risk given as the overall aim was to investigate how an individual would interpret their current family history situation.

It was assumed that many people understand that if they have a family history of certain conditions their insurance premium will be greater than for someone without such a family history. Therefore, having a family history in some circumstances may imply an increased risk for that person. For this analysis, each case was assigned a high, moderate or low risk assessment based on their family history, using the Scottish guidelines (Scottish Cancer Genetic Sub Group 2001).

Of the 1509 with family history data, 48 cases were assigned a moderate risk family history assessment because they were diagnosed with colorectal cancer under the age of 45. However, each of these 48 cases were the only person in the close family to be diagnosed with colorectal cancer and they would therefore answer 'no' to the question 'do you have family history of colorectal cancer?' Because of this they were omitted from the analysis. Therefore in total, 79 were omitted, leaving 1461 cases to be included in the remaining analysis.

Only 27 (1.8%) cases were assigned a high risk therefore, high and moderate risk cases have been combined creating two variables; those with a family history and those with no family history.

Another 5 cases did not respond to the question about the perceived presence of family history question and table 41 below, gives the distribution of 1456 cases by family history risk and perceived presence of a family history.

Table 41 Assigned family history risk and perceived presence of family history[18]

Assigned family history risk	Perceived family history (%)			
	YES	NO	Don't Know	Total
High or moderate	133 (59.9)	84 (7.3)	18 (20.0)	235
Low	89 (40.1)	1061 (92.7)	71 (80.0)	1221
	222	1145	89	1456

There was a statistically significant ($p<0.001$) difference between the cases in the three groups; those that did perceive they had a family history of colorectal cancer, those that did not perceive they had a family history of colorectal cancer and those that did not know if they had a family history of colorectal cancer and the assigned family history risk using Scottish guidelines.

Of those who did perceive they had a family history, 133 (59.9%) were assessed as having a high or moderate family history risk. In contrast, those who did not perceived

18 Perceived presence of family history – the perception of whether the case thought they had a family history of colorectal cancer

they had a family history, 84 (7.3%) cases were assessed as having a high or moderate family history risk, of cases who answered that they did not know if they had a family history 18 (20%) did have a high or moderate family history risk.

The same analysis was repeated for males 855 (58.4 %) and females 606 (41.6%) separately and the findings were similar to those described above. The 89 cases that answered 'don't know' to presence of a family history have been excluded in what follows leaving 1367 cases included in the analysis.

Deprivation scores

Table 42 below compares the relationship between the perceived presence of a family history and assigned family history risk in the 408 most affluent cases and 152 most deprived cases according to Carstairs deprivation index.

Table 42 Distribution of the perceived family history and family history risk by deprivation groups[19]

Deprivation groups	Assigned family history	Perceived presence of family history (%)	
		YES	NO
1 Most affluent	Moderate or High	38 (50.0)	25 (7.5)
	Low	38 (50.0)	307 (92.5)
3 More deprived	Moderate or High	17 (68.0)	8 (6.3)
	Low	8 (32.0)	119 (93.7)

19 Table 42 are the results using Carstairs deprivation groups 1 and 3

Of the most affluent group 38 (50%) cases perceived they had a family history of colorectal cancer but did not have an assigned high or moderate family history risk. However, only 8 (32%) cases in the most deprived group fell in to this category.

The same analysis was carried out using the SIMD index and the results were very similar.

Perceived presence of family history

The 222 cases that perceived presence of family history were asked if they discussed their family history concern with their GP. 215 cases answered this question and 7 cases omitted to answer. It was found that 76 (35.3%) cases had discussed their perceived presence of family history with their GP and 139 (64.7%) did not. Of the 76 cases discussing their concerns with their GP, 51 (67.1%) had a high or moderate family history risk assigned.

There was no statistically significant difference between males and females as to whether they discussed their concerns with a GP. Of the 117 cases that did discuss their concerns 60 (25.6%) were female and 57 (19.7%) were male.

Considering those with a perceived presence of family history, there was no statistically significant difference between the three deprivation categories (Carstairs index) in the proportion that discussed their concerns with their GP. Although statistically non significant, there was a trend using both deprivation indices, for the most affluent group to discuss their family history concerns with their GP. Using Carstairs index, 27 (35.5%) of the most affluent group and 7 (30.4%) of the most deprived group, and using SIMD

index 31 (36.9%) of the most affluent group and 5 (33.3%) of the most deprived, discussed their concerns.

Assigned family history risk

The family history results that have most clinical importance are those cases assigned a high or moderate family history risk (defined by the Scottish guidelines). These are an important group because the case is eligible for mutation analysis or microsatellite instability (MSI)[20] testing and their first-degree relatives eligible to enter a surveillance programme.

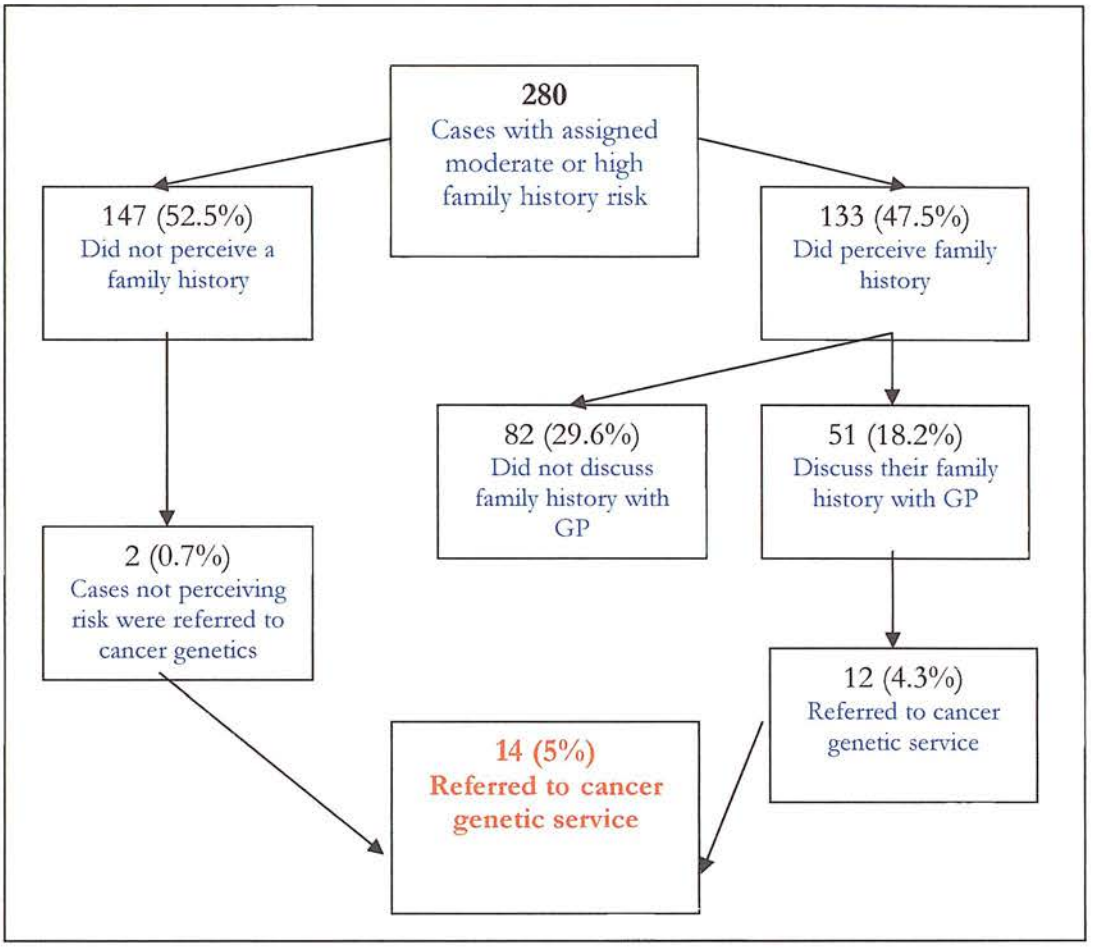
In this analysis there were a high proportion of cases with an assigned high or moderate family history not referred to a cancer genetic service. In this study 280 cases were assigned a high or moderate family history risk and were eligible for referral to cancer genetic services. Of the 280cases a total of 266 (95%) were not referred. Of these 280 cases, 147 (52.5%) did not perceive they had a family history, 83 (29.6%) of the 280 cases did perceive they had family history risk but did not discuss it with the GP.

Of the 280 cases with a high or moderate family history risk, 133 (47.5%) perceived they had a family history. Of these 133 cases that perceived a family history, 51 (18.2%) discussed their concerns with the GP. In the whole cohort, 6 other cases were referred to clinical genetics. However they all had a low risk family history.

20 Microsatellites sequences, short (1-6 nucleotide) sequences repeated tens to hundreds of times, occur normally in DNA. However, where DNA repair systems are abnormal, as when there are mutations in mismatch repair genes, abnormally long or short microsatellite sequences tend to accumulate. This phenomenon is termed microsatellite instability or MSI

Figure 17 demonstrates the numbers with family history and the final numbers referred to genetics.

Figure 17 ***280 cases with an increased family history risk of colorectal cancer and referral to cancer genetic services***



Referral to genetic department by GP

The 51 cases with a high or moderate family history risk that perceived a family history risk and had discussed the concern with their GP should have expected a referral to a cancer genetic clinic. When these cases were asked if they had been referred only 12 (23.5%) of the 51 cases with a high or moderate family history risk stated that they has been referred to a cancer genetic service.

When the relationship between assigned family history risk and referral to cancer genetic services was investigated, more females were referred. However, there was no statistically significant difference between sex and the proportion of those referred to cancer genetic services. Of those cases assigned a high or moderate family history risk and who perceived a family history risk 8 (13.8%) were females and 4 (6.6%) male.

There was a statistically significant ($p<0.001$) difference found between the proportions of cases referred to cancer genetic services in the different age group. Cases in the youngest age group (16-54) were most likely to be referred to cancer genetic services. In the younger age group, 8 (18.6%) cases were referred, in the middle age group 2 (6.5%) were referred and 2 (4.4%) in the older age group were referred. However it is acknowledged that the numbers of cases in each age subgroup are very small.

There was no statistically significant difference found between the proportions referred to cancer genetics services and the deprivation groups using both deprivation indices. Of those cases with an assigned high or moderate family history risk referred to the cancer genetic services 5 (11.1%) are in the most affluent group, 6 (8.7%) in the moderate group and 1 (20%) in the most deprived group using Carstairs deprivation index. Using the SIMD deprivation index and the group of cases with an assigned high or moderate family history risk referred to the cancer genetic services, 6 (10.9%) are in the most affluent group, 6 (9.7%) in the moderate group and 0 (0%) in the most deprived group. It is acknowledged that the numbers are small and there is low power to detect a difference.

Dukes' Staging

Relationship analysis was carried out to identify any differences in Dukes' staging and cases with an assigned high or moderate family history risk, No statistically significant difference between cases with a high or moderate family history and the Dukes' stage of tumour at diagnosis was found. The results shown in table 43 are for total number of 1140 cases that had Dukes' staging available for analysis.

Table 43 Cases with an assigned high or moderate family history risk and Dukes' stage at presentation

Family history risk	A	B	C	D
High or Moderate	45 (22.6)	72 (34.0)	80 (37.0)	8 (3.8)
Low	196 (20.6)	357 (37.5)	345 (36.2)	37 (3.9)

There was no statistically significant difference between those with a high or moderate family history risk and those that a perceived family history risk in the proportions referred to hospital after one or more than one visit to GP.

Perceived presence of colorectal cancer family history

As not all of the cases with a high or moderate family history risk perceived a family history of colorectal cancer, the following analysis was carried out using only the 222 cases that did perceive a family history of cancer. The analysis was to ascertain if a perceived family history of colorectal cancer initiated a different behaviour pattern than those cases with no perceived family history risk.

There was a statistically significant ($p<0.001$) difference between the proportion of cases with a perceived family history of colorectal cancer and those not perceiving a family history colorectal cancer stating 'some knowledge of colorectal cancer'. Those with a perceived family history of colorectal cancer were more likely to state 'some knowledge' of colorectal cancer symptoms than those not perceiving a family history. In the group perceiving a family history of colorectal cancer 130 (56.8%) had 'some knowledge' of colorectal cancer symptoms and those with no perceived family history risk 521 (43.1%) stated they had some had 'some knowledge' of colorectal cancer symptoms.

There was a statistically significant ($p<0.001$) difference between the proportion of cases with a perceived family history of colorectal cancer and those not perceiving a family history colorectal cancer when asked about whether they considered that they had cancer before their diagnosis. Of the cases that perceived a family history risk 119 (52%) considered cancer before diagnosis and of those not perceiving a family history risk 443 (36.9%) considered cancer before diagnosis. There was no statistically significant difference between cases with a perceived family history of colorectal cancer and those not perceiving a family history colorectal cancer and the waiting time with symptoms or likelihood of self medicating for symptoms or discussing symptoms with another person before visiting their GP. Table 44 shows the mean waiting time for each symptom of those cases perceiving and not perceiving a family history of colorectal cancer

Table 44 ***Median waiting time with symptoms of cases perceiving and not perceiving a family history of colorectal cancer***

Symptoms	Median wait time for cases perceiving family history (days)	Median wait time for cases not perceiving family history (days)
Change in bowel habit	84	61
Rectal bleeding	61	42
Weight loss	121	90
Marked loss of energy	91	91
Wind and bloating	91	70
Loss of appetite	61	61
Mucus	56	61
Tenesmus	28	61
Abdominal discomfort	61	61
Pain	30	21
Nausea	60	21
Vomiting	43	7

It can be seen in table 44 that although not statistically significant those cases not perceiving a family history risk of colorectal cancer were more likely to visit the GP sooner than those that did perceived they had a family history risk of colorectal cancer.

There was no statistically significant difference between the response of those cases that did and did not perceive a family history of colorectal cancer to the question asking if they discussed their symptoms with anyone prior to visiting the GP. Of the cases that did perceive a family history 137(14.3%) did discuss their symptoms with someone and 69(14.4%) cases did not discuss their symptoms with anyone.

There was no statistically significant difference between the response of those cases that did perceive a family history risk of colorectal cancer to the question asking if they had taken any over the counter medication for any symptom prior to visiting the GP and the cases that did not perceive a family history of colorectal cancer. Of the cases that did

perceive a family history 39 (12.8%) did take medication for a symptom and 167 (14.9%) cases did not take medication for any symptom prior to visiting their GP.

Chapter 14

Results: Symptom presentation

Lower gastrointestinal symptom

Cases were asked if they had visited their GP to discuss the presenting symptom that concerned them. A total of 1533 responded to this question. Of the 1533 cases **1212** (79.0%) did visit a GP to discuss their symptom, another **112** (7.3%) cases stated that they had gone to their GP for another reason and mentioned that they had a lower gastrointestinal symptom and **87** (5.7%) cases did not visit a GP and were referred for further investigation from another hospital appointment or diagnosed with colorectal cancer whilst attending another hospital appointment. A further 122 (8.0%) did not visit their GP with symptoms, as they did not think they had symptoms requiring a visit to a GP.

Of these 122 cases that did not a visit to a GP with symptoms, 100 cases were investigated for colorectal cancer during a faecal occult blood testing (FOBT) pilot (48 of these cases did report having symptoms to research nurse) and 22 were a mixture of just feeling generally unwell when they visited the GP or were admitted after a collapse but reported no symptom. Of the total 199 that were referred from another hospital appointment or did not present to a GP, 115 had symptoms and are included in table 46.

A total of 1324 case did discuss symptoms with their GP. The main presenting symptom is given in table 45.

Table 45 Presenting symptoms that prompted first visit to GP

Symptom	Cases with symptom	
	1324	(%)
Rectal bleeding	492	(37.2)
Change in bowel habit	349	(26.4)
Abdominal pain	220	(16.6)
Marked loss of energy/ breathlessness	139	(10.5)
Family history	87	(6.6)
Weight loss	20	(1.5)
Tenesmus	3	(0.2)
Other	14	(0.7)

This table illustrates that rectal bleeding and change in bowel habit are the two most common symptoms that prompt presentation to the GP.

After asking the question on the main symptom that prompted their visit to the GP, all 1540 cases were asked by the research nurse to state whether they had experienced any of a list of symptoms before visiting their GP. For each symptom reported they were asked how long it had been present when they first visited their GP. Many cases presented with several symptoms at the first GP visit therefore, the total number with symptoms in table 46 is higher than the total number of cases.

Table 46 Percentage of cases with each symptom

Symptom	Number of cases responding to question	Number in cohort with symptom	(%)
Change in bowel habit	1501	805	(53.6)
Rectal bleeding	1491	768	(51.5)
Weight loss	1491	256	(17.2)
Marked loss of energy	1489	603	(40.5)
Wind and bloating	1501	506	(33.7)
Loss of appetite	1499	246	(16.4)
Mucus	1490	296	(19.9)
Tenesmus	1484	324	(21.8)
Abdominal discomfort	1499	346	(23.0)
Pain	1489	332	(22.3)
Nausea	1333	159	(11.9)
Vomiting	1337	123	(9.3)

Table 46 shows that greater than 50% of cases in the whole cohort were experiencing either rectal bleeding or a change in bowel habit when they first presented to a GP. Change in bowel habit, rectal bleeding and marked loss of energy were the 3 symptoms experienced by the highest percentage of individuals in the whole cohort and by site of cancer. There was no statistically significant difference between males and females in the frequency of those experiencing rectal bleeding or a change in bowel habit. Of 603 experiencing a marked loss of energy, there was a statistically significant difference ($p<0.001$) between the sexes and the numbers reporting this symptom. Females were more likely to report having marked loss of energy, 299 (48.1%) females reported this and 304 (35%) of males.

There was no statistically significant difference between the age groups in the proportion of those with or without a change in bowel habit. There was a statistically significant difference between the age groups and the reporting of rectal bleeding

($p<0.001$) and marked loss of energy ($p<0.05$) where the youngest age group (16-54) were more likely to report these symptoms.

In the youngest age group (16-54) rectal bleeding was reported by 191 (63.9%) cases and reported by (46.7%) in the older age group (65-80). Marked loss of energy was reported by 140 (47.3%) of the younger age group and 294 (38.5%) of the oldest age group (65-80).

There was no statistically significant difference between those with or without rectal bleeding, change in bowel habit and marked loss of energy within the deprivation groups using both indices. When the same analysis was carried out using colon and rectal cancer data separately the results remain statistically non significant for both.

Other symptoms

All cases were asked if they had any other symptoms they would like to mention that were not included on the list. 184 (11.9%) of all cases stated they had another symptom. The more common symptoms reported are listed below:

- Breathlessness 37 (20.1%)
- Indigestion 24 (13.0%)
- Dizzy 13 (7.1%)
- Thinner stools 11 (6.0%)
- Foul smelling stools 8 (4.3%)
- Felt a lump 7 (3.8%)
- Back pain 6 (3.3%)
- Various other symptoms 78 (38.6%)

Site of cancer

The site of cancer was available for 1199 cases. Of the 1199 cases, 44 (3.6%) had a double primary tumour. There were 697 (58.1%) cases with colon cancer and 502 (41.9%) with rectal cancer. Rectal cancers include the recto-sigmoid cancers.

The sex distribution in colon cancer was 55.4% male and 44.6% female. There was a statistically significant difference ($p<0.05$) between distribution of sex and site of cancer. Of those with rectal cancer there were 312 (62.2%) males and 190 (37.8%) females. There was no statistically significant difference between site of cancer and age groups or different deprivation groups (using both deprivation indices). There was a trend that the most affluent group were more likely to be diagnosed with rectal cancer and the most deprived group diagnosed with colon cancer (using both deprivation indices). Table 47 is the results of cancer site and Carstairs deprivation index.

Table 47 Site of cancer and Carstairs deprivation groups

	Colon		Rectum	
Deprivation group	number	(%)	number	(%)
1	205	(59.4)	140	(40.6)
2	387	(55.7)	308	(44.3)
3	89	(66.4)	45	(33.6)

Table 48 presents a comparison of symptoms at presentation to a GP by rectal and colon cancer, some cases had more than one symptom. The table also presents the difference in the proportions (all calculations relate to rectal cancer from colon cancer). The 95% confidence intervals (CI) given in table 48 are the confidence intervals for the difference in proportions.

Table 48 Site of cancer and symptom presentation

Symptom	Site of Cancer					
	Colon		Rectum		Difference in proportions	95% Confidence Interval of the difference
	697	(%)	502	(%)		
Change in bowel habit	317	(45.5)	307	(61.2)	-0.157	-0.212 to -0.100
Rectal bleeding	237	(34.0)	370	(73.7)	-0.397	-0.447 to -0.343
Weight loss	132	(18.9)	73	(14.5)	0.044	0.001 to 0.086
Marked loss of energy	310	(44.5)	152	(30.3)	0.142	0.087 to 0.195
Wind & bloating	232	(33.3)	168	(33.5)	-0.002	-0.056 to -0.052
Loss of appetite	143	(20.5)	51	(10.2)	0.104	0.063 to 0.143
Mucus	99	(14.2)	130	(25.9)	-0.117	-0.142 to -0.071
Tenesmus	113	(16.2)	141	(28.1)	-0.119	-0.167 to -0.071
Abdominal discomfort	177	(25.4)	83	(16.5)	0.089	0.042 to 0.134
Pain	194	(27.8)	67	(13.3)	0.145	0.099 to 0.189
Nausea	92	(13.2)	28	(5.6)	0.076	0.043 to 0.108
Vomiting	74	(11.0)	14	(2.8)	0.078	0.051 to 0.106

This table demonstrates the differences in symptom presentation with the site of colorectal cancer. The most common symptom for colon cancer is change in bowel habit. Also noted is the high proportion with marked loss of energy in colon cancer cases. In cases with rectal cancer, rectal bleeding was the most common symptom.

There was no statistically significant difference between delay in presentation with symptoms and site of cancer. However there was a difference in the delay pattern and site with most symptoms. Table 49 presents the results of each symptom and waiting with symptoms less than six weeks and greater than six weeks.

Table 49 Delay time reporting symptoms and site of cancer

Symptoms	Site of Cancer			Site of Cancer	
	Colon < 6 weeks	Rectum < 6 weeks		Colon > 6 weeks	Rectum > 6 weeks
Change in bowel habit	118 (39.3)	93 (32.3)		182 (60.7)	195 (67.7)
Rectal bleeding	128 (54.9)	175(47.6)		105 (45.1)	193 (52.4)
Weight loss	23 (18.3)	19 (27.1)		103 (81.7)	51 (72.9)
Marked loss of energy	78 (25.4)	35 (23.2)		229 (74.6)	116 (76.8)
Wind & bloating	66 (30.0)	48 (29.6)		154 (70.0)	114 (42.5)
Loss of appetite	53 (39.3)	17 (33.3)		82 (60.7)	34 (66.7)
Mucus	35 (37.2)	55 (45.8)		59 (62.8)	65 (54.2)
Tenesmus	38 (35.5)	45 (33.8)		69 (64.5)	88 (66.2)
Abdominal discomfort	68 (42.8)	25 (33.8)		91(57.2)	49 (66.2)
Pain	107 (63.3)	33 (57.9)		62 (36.7)	24 (42.1)
Nausea	52 (59.1)	13 (50.0)		36 (40.9)	13 (50.0)
Vomiting	52 (70.3)	9 (69.2)		22 (29.7)	4 (30.8)

Six weeks was chosen for this analysis because is the time scale stated in the referral guidelines 'for suspected colorectal cancer' that key symptoms should be present in an individual before being referred for further investigation.

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Low haemoglobin levels and colorectal cancer site

There was a difference in the distribution of low haemoglobin levels and site of colorectal cancer. In male colon cancers 80 (77.6%) had haemoglobin levels less than 11g/dl and only 23 (22.4%) of rectal cancers. Of females with colon cancer 51 (87.9%) had haemoglobin levels less than 10g/dl and 7 (12.1%) with rectal cancers. All females with low haemoglobin levels are included in this analysis, not only post-menopausal women.

Table 50 shows the median waiting times in weeks for whole cohort before seeing a GP.

Table 50 Waiting time with symptoms (Median, 25th and 75th centiles)

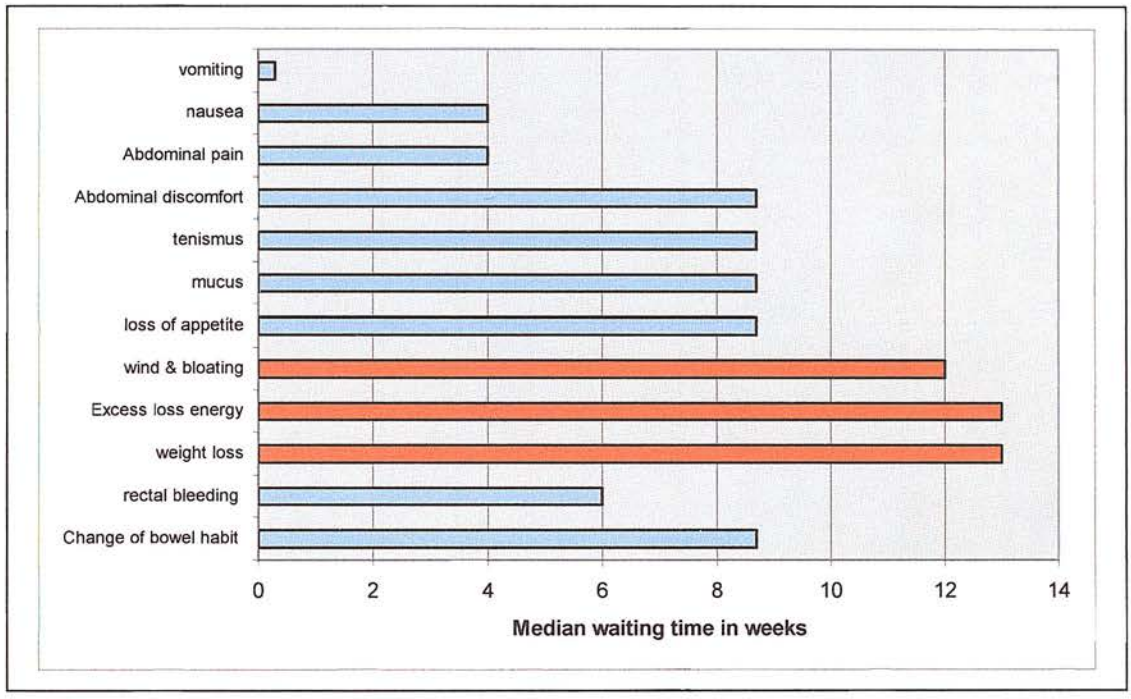
Symptom	Median waiting time whole cohort	25th-75th Centiles	Median waiting time for colon cancer	25th-75th Centiles	Median waiting time for rectal cancer	25th-75th Centiles
Change in bowel habit	**8.7**	4.0 - 26.0	**8.7**	3.0 - 26.0	**11.0**	4.2 - 26.0
Rectal bleeding	**6.0**	2.0 - 21.7	**4.3**	1.0 - 21.7	**8.0**	2.0 - 25.3
Weight loss	**13.0**	8.0 - 26.0	**13.0**	8.6- 26.0	**8.70**	8.7 - 26.0
Marked loss of energy	**13.0**	6.0 - 26.0	**13.0**	6.0 - 26.0	**13.0**	8.0 - 26.0
Wind and bloating	**12.0**	4.2 - 26.0	**12.0**	4.2 - 26.0	**12.0**	4.2 - 26.0
Loss of appetite	**8.7**	4.0 - 17.4	**8.7**	4.0 - 17.4	**8.7**	4.2 - 17.4
Mucus	**8.7**	4.0 - 17.4	**8.7**	4.0 - 26.0	**8.3**	3.0 - 17.4
Tenesmus	**8.7**	4.2 - 21.7	**8.7**	4.2 - 26.0	**8.7**	4.2 - 21.7
Abdominal discomfort	**8.7**	3.7 - 26.0	**8.7**	3.0 - 26.0	**10.8**	4.3 - 26.0
Pain	**4.0**	1.0 - 13.0	**4.0**	0.6 - 13.0	**4.2**	1.1 - 11.4
Nausea	**4.2**	1.0 - 13.0	**4.0**	0.7 - 13.0	**6.4**	1.0 - 12.9
Vomiting	**1.4**	0.28 - 8.7	**2.0**	0.28 - 8.7	**1.0**	0.28 - 9.3

This table shows that weight loss, marked loss of energy, wind and bloating were the three symptoms present for the longest time at first visit to a GP.

Cases with colon cancer waited a shorter time that those with rectal cancer. Rectal cancer cases with rectal bleeding wait 8 weeks and those with a change in bowel habit waited 11 weeks before visiting a GP. Colon cancer cases waited 8.7 weeks with rectal bleeding and 4.3 weeks with a change in bowel habit.

Figure 18 visually illustrates the median waiting time with each symptom.

Figure 18 Median waiting times for cohort before seeing GP



The cumulative numbers and percentages of cases waiting various times with each symptom are shown in table 51. The number of cases with the symptoms, shown in table 40 differs slightly from those who gave the waiting time as, some cases failed to give a waiting time although the symptom was present.

It was interesting to look at the cumulative waiting time with symptoms before visiting a GP and these are shown in table 51.

Table 51 Percentage of cases and cumulative waiting times with symptoms before visiting GP

Symptoms	Median wait (weeks)	Number with symptom	Waiting at least 4 weeks to report symptoms	% Reporting symptoms by 4 weeks	Waiting at least 12 weeks to report symptoms	% Reporting symptoms by 12 weeks	Waiting at least 24 weeks to report symptoms	% Reporting symptoms by 24 weeks	Waiting at least 52 weeks to report symptoms	% Reporting symptoms by 52 weeks
Change in bowel habit	8.7	755	230	(26.9)	429	(53.3)	577	(72.9)	684	(87.1)
Rectal bleeding	6	755	316	(41.9)	486	(64.4)	576	(76.3)	672	(89.0)
Weight loss	13	244	24	(9.8)	118	(48.3)	168	(68.8)	220	(90.1)
Marked tiredness	13	596	97	(16.3)	266	(44.7)	404	(67.9)	512	(86.0)
Wind and bloating	12	483	98	(20.3)	243	(50.3)	344	(71.2)	429	(88.8)
Appetite	8.7	239	63	(26.4)	143	(59.9)	190	(79.6)	228	(95.5)
Abdominal discomfort	8.7	314	93	(29.6)	176	(56.0)	230	(73.2)	276	(87.8)
Pain	4.0	296	159	(53.7)	220	(74.3)	250	(84.4)	274	(92.5)
Nausea	8.7	151	75	(49.7)	110	(72.9)	126	(83.5)	142	(94.1)
Vomiting	1.4	119	78	(65.5)	94	(79.0)	109	(91.6)	114	(95.8)

This table illustrates that on average 25% of cases waited up to 24 weeks to visit their GP with symptoms. No statistically significant difference between waiting time with symptoms and sex, age, with or without comorbidity, deprivation groups (using both deprivation indices) were detected using Spearman's rank correlation.

Analysis was carried out on the site of cancer and waiting time with rectal bleeding, change in bowel habit and weight loss because the median wait time differed by site for these symptoms. The results showed no significant difference for any of the analysis with the exception of rectal bleeding and age. The younger the age of person with rectal bleeding the longer they wait to report symptoms.

Multivariate analysis

In addition to the above analysis, a multivariate model was built using Cox proportional hazard modelling. The models were built and fitted to the data to investigate differences between age, sex, comorbidity and deprivation, to determine the likelihood that someone would present to the GP with rectal bleeding, change in bowel habit or marked loss of energy. For each symptom two models were created for each of the deprivation indices together with age, sex and number of comorbidities. None of the variables were associated with the likelihood of presenting with rectal bleeding. For change in bowel habit there was a positive association with age ($p=0.006$). For an increase in age of 10 years, the hazard of presenting with change in bowel habit was increased by a factor of 1.12 (95% CI 1.03, 1.22). For marked loss of energy there was a difference between the sexes ($p=0.003$) the male to female hazard ratio was 0.76 (95% CI 0.63, 0.91). Therefore, males are 25% less likely to present with marked loss of energy. Models were built using cases with rectal and colon cancer separately and the

analysis results were identical to those described above. Following these results using the more common presenting symptoms a decision was taken not to proceed further with more multivariate analysis.

Total number of symptoms at first visit to GP

The total numbers of symptoms at presentation to a GP was not normally distributed and a median of 3 symptoms present at first visit to a GP was found, inter-quartiles (1-4). Of the 1540 cases, 99 reported no symptoms and 48 were cases found at FOBT pilot, the remaining 51 cases were a combination of cases found at a surveillance appointment for previous colorectal cancer, ulcerative colitis and polyps. In addition some patients were already inpatients for other reasons and underwent a colonoscopy. This figure differs from those who did not present with symptoms to their GP as 23 cases not visiting their GP reported having symptoms before any investigation. Figure 19 shows the total number of symptoms at presentation.

Figure 19 ***Distribution of recruited patients with colorectal cancer by number of lower gastrointestinal symptoms at presentation***

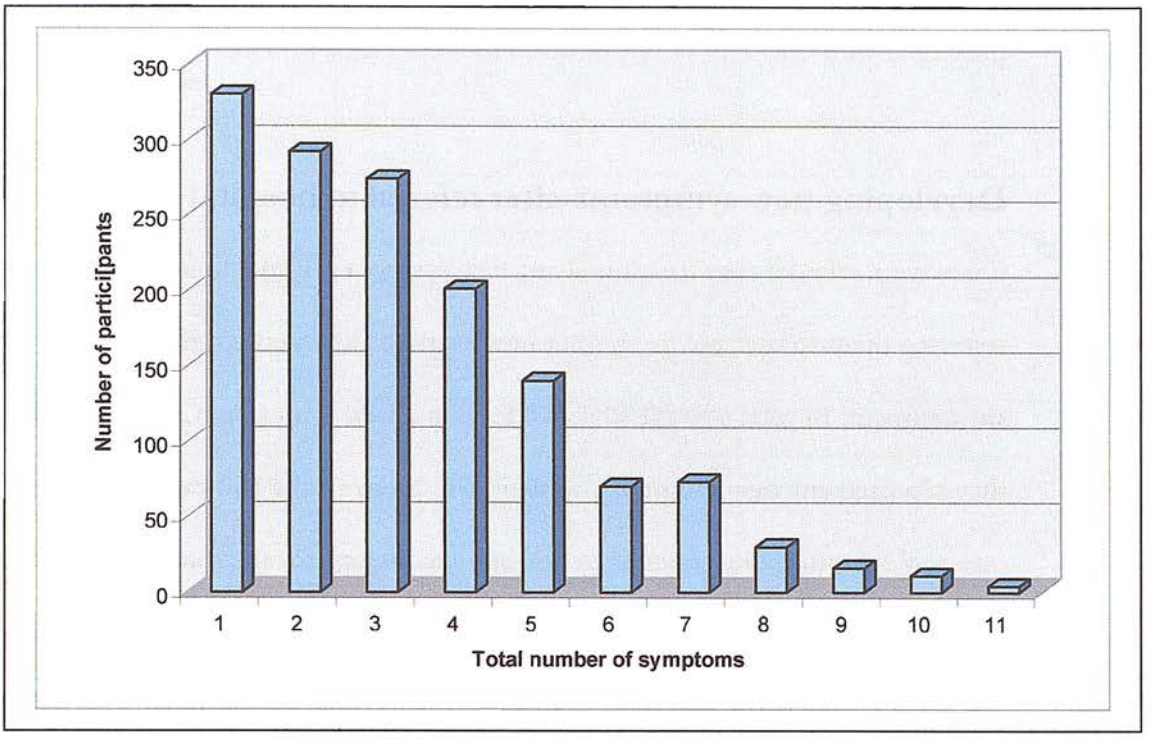


Figure 19 shows that the majority of cases presented with between 1 and 3 symptoms. The following analysis was carried out after classifying the cases into 2 groups according to whether they had 1-3 symptoms or 4-11 symptoms. There was a statistically significant ($p<0.001$) difference between the sexes in the proportions that has 1-3 symptoms and those that had 4-7 symptoms at presentation to GP. Males were more likely to be in the group with a higher number of symptoms. Results show that there were 255 (42.5%) females in the group with 1-3 symptoms and 267 (32.4%) males in this group.

There was no statistically significant difference between the age groups or deprivation groups in the proportions of those with 1-3 symptoms at presentation to GP or those with 4-11 symptoms at presentation to GP.

Of the 333 cases presenting to GP and reporting only one symptom, the highest percentage consisted of rectal bleeding (162 (48.6%)), marked loss of energy (67 (20.1%)) and change in bowel habit (57 (17.1%)) the remaining 47 (14.1%) cases presented with only one symptom from the other nine possible remaining symptoms.

Developing new symptoms after referral to hospital

Cases were asked if they developed any new symptoms in the time between their GP referring them to hospital for further investigations and getting their hospital appointment. In total 490 (31.8%) did develop a new symptom. Cases were also asked if they reported any new symptoms to their GP. Many of the 490 cases develop more than one new symptom after referral to hospital accounting for the total number in table 52 being greater than 490 cases. Table 52 shows the number that developed each symptom and the number of the 490 cases that discussed the new symptom with their GP.

Table 52 ***New symptoms developing after referral to hospital and the number reporting new symptoms to GP***

New symptom	Number with new symptom	(%)	Number reporting new symptom to GP	(%)
Change in bowel habit	125	(25.5)	77	(61.6)
Rectal bleeding	94	(19.1)	63	(67.0)
Marked loss of energy	93	(19.0)	40	(43.0)
Weight loss	78	(15.9)	40	(51.2)
Wind & bloating	68	(13.9)	30	(44.1)
Loss of appetite	65	(13.2)	29	(44.6)
Mucus	60	(12.2)	32	(53.3)
Tenesmus	55	(11.9)	28	(50.9)
Abdominal discomfort	50	(10.9)	27	(54.0)
Pain	93	(19.1)	65	(69.8)
Nausea	52	(10.6)	36	(69.2)
Vomiting	52	(10.6)	38	(73.0)

This table shows that approximately one third of cases developed new symptoms whilst waiting for a hospital appointment. Of those with new symptoms, 48 (38.4%) cases with change in bowel habit, 31 (33%) with rectal bleeding and 53 (57%) with marked loss of energy did not report these to their GP. There was no statistically significant difference in sex of cases between those reporting new symptoms to their GP and not reporting symptoms. There was a statistically significant ($p<0.05$) difference between age groups in those reporting new rectal bleeding. There was a statistically significant ($p<0.01$) difference between age groups in those reporting new change in bowel habit and a statistically significant ($p<0.001$) difference between age groups in those reporting new marked loss of energy. The results of this analysis are shown in Table 53.

Table 53 ***Percentage within each age group that reported new symptoms to GP after referral to hospital***

Age group	Percentage in age groups reporting new symptoms		
	Rectal bleeding ($p<0.05$)	Change in bowel habit ($p<0.01$)	Marked loss of energy ($p<0.001$)
16-54	13 (68.4%)	19 (70.4%)	14 (60.9%)
55-64	21 (50.0%)	25 (152.1%)	10 (30.3%)
65-80	31 (40.3%)	33 (38.4%)	17 (20.5%)

This table shows that a higher proportion of young people who develop a new symptom reported this to their GP.

Anal symptoms

Cases were asked if they experienced any symptoms in their anal region such as; itching, soreness, lumps, discomfort, pain or anything prolapsed and 1347 responded. Of those who responded, 1094 (81.2%) had no anal symptoms and 289 (18.8%) had anal symptoms.

Of the 289 who did have anal symptoms, 253 gave the symptom they had experienced:

- Soreness 78 (27.5%)
- Itching 118 (41.5%)
- Lumps 43 (14.8%)
- Discomfort 75 (25.7%)
- Pain 59 (20.1%)
- Prolapse 14 (4.6%)

Itching was the most common symptom experienced by 118 (41.5%) cases. A number of cases had more than one anal symptom.

Of the 768 cases with rectal bleeding, 512 (66.7%) had no anal symptoms. These represented 512 (35.6%) of cases from the 1439 that answered both questions on rectal bleeding and anal symptoms.

Specific information on change in bowel habit

Of the 1540 cases, 805 (53.6%) cases reported having a change in bowel habit. These cases were asked to give more specific information on the frequency and consistency of this change. Of those with a change in bowel habit, 743 cases gave information on change of frequency, 473 (63.7%) had increased frequency, 200 (26.9%) decreased frequency and 70 (9.4%) reported having both increased and decreased frequency.

Cases with increased frequency were asked about consistency and 430 case of the 473 replied. Of the 430 cases, 416 (89.1%) cases reported that with the increased frequency they also had looser stools.

Of 805 cases reporting change in bowel habit, the total number with change to increased and/or looser stools was 549 (68.2%) cases.

Self treatment

Cases were asked if they had self-treated for any symptom before visiting the GP, 1127 responded to this question. Of these, 305 (27%) stated they had taken medication for a symptom. Of the 305 that did self-treat, 298 stated which symptom they had treated and these are shown in table 54.

Table 54 ***Number and (percentage) of patients with colorectal cancer that self treated before presentation by specific symptom***

Symptom	Cases that self treated symptoms	
	N=298	(%)
Change in bowel habit	137	(46.0)
Pain	52	(17.4)
Piles	48	(16.1)
Wind	20	(6.7)
Itching	15	(5.0)
Indigestion	11	(3.4)
Nausea	5	(1.7)
Other	10	(3.7)

This table shows that the most common symptom to self-treat was a change in bowel habit.

There was no statistically significant difference between the percentages of males and females that self-treated or within deprivation groups. There was a statistically significant difference ($p<0.001$) between the proportion in the age groups and those self-medicating. Of all three age groups, the youngest age group (16-54) was more likely to take medication for a symptom. Of those who stated that they self-treated there were 82 (26.5%) in the younger and 130 (16.5%) in the oldest age group (65-80).

Discussion of symptoms with other people

Cases were asked if they discussed their symptoms with anyone before visiting the GP. 1397 responded and 963 (68.9%) stated that they had discussed their symptoms with someone. If they had discussed their symptoms they were asked the relationship of the person they discussed symptoms with and 945 gave the relationship of the person. Of

these, 689 (72.9%) stated they had discussed symptoms with their spouse or partner, 232 (24.6%) with another family member and only 10 (1%) with a health professional such as a pharmacist or nurse.

There was a statistically significant difference ($p<0.007$) in the proportion of males and females discussing their symptoms with someone. Males were more likely than females to discuss their symptoms. The number of males discussing symptoms with someone were 582 (69.5%) compared to 381 (62.8 %) females. Younger cases were more likely that older cases to discuss their symptoms with someone but this was not statistically significant. In the younger age group 207 (71.3%) discussed their symptoms compared to 474 (64.1%) of the older age group.

Waiting time with any symptoms.

At commencement of this study the referral guidelines for the management of colorectal cancer available to GPs in Scotland stated if a symptom was present for more than 4 weeks the patient should be referred for investigations (SIGN 1997).

If the case had waited more than 4 weeks with any symptom, the research nurse asked the case if there was any reason why they waited more than 4 weeks.

For 411 cases it was not applicable to ask the question, as they did not have any symptom for more than 4 weeks. Of 1129 asked a total of 952 gave a reason or made a statement. The responses for waiting more than 4 weeks with a symptom are shown in table 55

Table 55 ***Reasons given for waiting more than 4 weeks with symptoms before reporting to GP***

Reason for waiting > 4weeks	Number	
	952	(%)
Thought had piles	140	(14.7)
Symptoms vague, intermittent	109	(11.4)
Hoped symptom would go away	94	(9.9)
No reason really	70	(7.4)
Did not think it was serious	54	(5.7)
Inflammatory bowel disease	52	(5.5)
Ageing process	34	(3.6)
Did not want to bother GP	30	(3.2)
Too Frightened or embarrassed	28	(2.9)
Too busy	21	(2.2)
Caring for a dying close relative	18	(1.9)
Not aware being tired could be a symptom of anything	18	(1.9)
Constipation before	15	(1.9)
Other	269	(28.3)

Table 55 demonstrates that there are a wide variety of reasons for cases waiting with symptoms before visiting their GP. The most common reason for waiting was that people believed that their symptoms to be related to having piles.

There was a statistically significant ($p<0.05$) difference between the age groups and those waiting more than 4 weeks before visiting a GP with symptoms, and those not waiting more than 4 weeks before visiting a GP. In the younger age group 198 (77.3%) cases presented after 4 weeks opposed to 483 (68.1%) of the older age group. This younger age group were also more likely to associate their symptoms to piles than the

older age group, In the younger age group the number thinking they had piles was 36 (18.2%) and in the older age group 59 (12.2%).

Inspecting the toilet before flushing

Cases were asked if, before their diagnosis of colorectal cancer, they looked down the toilet before they flushed and also asked, if they looked at the toilet paper before flushing. The responses to these questions are shown in Table 56.

Table 56 Number and (percentage) of patients with colorectal cancer who inspected the toilet and toilet paper by frequency of inspection

Frequency	Looking down toilet		Looking at toilet paper	
	N=1080	(%)	N=1055	(%)
Every time	668	(61.9)	683	(64.7)
Once a week	38	(3.4)	33	(3.1)
Once a month	3	(0.3)	5	(0.5)
Sometimes	371	(34.4)	334	(31.7)

This table shows that a high proportion of individuals do inspect the toilet and the toilet paper before flushing.

Inspecting down the toilet

There was a statistically significant difference ($p<0.01$) in the proportion of males and females that inspect the toilet before flushing. Males were more likely to inspect the toilet than females, 662 (73.7%) males reported inspecting the toilet and 425 (66.5%) of females. There was also a statistically significant difference ($p<0.001$) between the proportions in the age groups inspecting the toilet before flushing. The younger age

group (16-54) were more likely to do so; 243 (78.9%) of the younger age group did inspected the toilet compared to 533 (67.5%) of the older age group (65-80).

There was a statistically significant difference ($p<0.05$) between the deprivation groups and inspecting the toilet. Using both deprivation indices the most affluent group were more likely to inspect the toilet before flushing than the most deprived group. The analysis results using the Carstairs index found that in the most affluent group 309 (74.5%), the middle deprivation group 647 (71%) and only 130 (61.9%) in the most deprived group inspected the toilet before flushing. Using the SIMD index 352 (75.2%) of the most affluent group, 651 (69.2%) of the middle group and only 82 (65.1%) of the most deprived group inspect the toilet before flushing.

Inspecting the toilet paper

There was no statistically significant difference between the proportions of males and females inspecting the toilet paper before flushing. There was a statistically significant difference ($p<0.001$) in proportions within the age groups inspecting the toilet paper; the younger age group were more likely to inspect the toilet paper before flushing. There were 249 (81.1%) of the younger age group and 524 (67.1%) of the older age group who inspected the toilet paper before flushing.

There was a statistically significant difference ($p<0.001$) between the deprivation categories and those inspecting the toilet paper before flushing. Using both deprivation indices the most affluent group were more likely than the most deprived group to inspect the toilet paper before flushing. Using the Carstairs index it was found that of the most affluent group 316 (76.5%), the middle group 620 (69%) and most deprived

group 127 (60.5%) inspected the toilet paper before flushing and using the SIMD index, of the most affluent group 357 (76.6%), the middle group 622 (67.7%) and the most deprived group 77 (61.1%) inspect the toilet paper before flushing.

Number of visits to GP before referral to hospital

Cases were asked to state how many visits they made to see their GP before they were referred to hospital for further investigations. A total of 1327 cases replied, 723 (54.5%) were referred after their first visit, 440 (33.2%) after 2 or 3 visits, 93 (7.0%) after 4 or 5 visits and 71 (5.4%) were referred after more than 5 visits to the GP.

Classifying the cases into two groups according to whether they were referred to hospital after one visit to GP or more than one to GP, there was no statistically significant difference between the sexes, the age groups, the deprivation groups, the knowledge groups or those with comorbidity or without comorbidity in the proportions referred to hospital after one visit to GP. Although not statistically significant, there were a greater number of cases in the most affluent group (using both deprivation indices) that were referred on their first visit to their GP than the most deprived group. Results for both deprivation indices are shown in table 57.

Table 57 Referral to hospital on first visit to GP by deprivation group

	Deprivation Index	
Deprivation group	**Carstairs**	**SIMD**
1 (most affluent)	192 (56.8%)	224 (56.9%)
2	439 (54.9%)	440 (53.9%)
3 (most deprived)	92 (48.9%)	59 (51.8%)

Using the data from table 57 chi square for trend was carried out and the results remained statistically non significant.

Knowledge of colorectal cancer symptoms

Cases were asked to describe their own knowledge of colorectal cancer symptoms before their diagnosis. 1529 responses were as follows in Table 58.

Table 58 ***Knowledge of colorectal cancer symptoms before diagnosis***

Responses	Number	%
None	847	(55.4)
A little	518	(33.9)
Good	121	(7.9)
Very good	37	(2.4)
Expert	6	(0.4)

Table 58 notes that 55% of cases in this study stated they had no knowledge of colorectal cancer symptoms before their diagnosis.

There was no statistically significant difference between proportions in age groups; however the older age group were more likely than the younger age group to state they had no knowledge of colorectal cancer symptoms. There were 451 (57.1%) of the older group stating no knowledge and 162 (52.4%) in the younger group.

There was a statistically significant difference ($p<0.001$) between the knowledge of colorectal cancer before diagnosis and sex of cases. Males were more likely to state they had 'no knowledge' of colorectal cancer symptoms before their diagnosis than females.

There were 532 (59%) males reporting 'no knowledge' and 315 (49.3%) of females reporting 'no knowledge' of colorectal cancer symptoms. Table 59 shows the numbers and percentages within the deprivation groups for both deprivation indices and knowledge of colorectal cancer symptoms.

Table 59 Knowledge of colorectal cancer before diagnosis with deprivation groups

Deprivation group	No Knowledge of symptoms	
	Carstairs (%)	SIMD (%)
1 (most affluent)	199 (47.7)	217 (46.2)
2	492 (53.9)	533 (56.6)
3 (most deprived)	155 (73.8)	96 (76.2)

Was cancer considered before diagnosis?

Cases were asked if they considered having cancer before their diagnosis. Of the total 1540 cases, 1530 answered this question, 605 (40%) did consider cancer and 925 (60%) did not consider cancer.

Of cases the 605 cases that considered they had cancer before diagnosis, 589 cases reported at which stage before their diagnosis this was considered. The responses were as follows:

- 298 (50.6%) thought this before they attended their GP,
- 125 (21.2%) after tests were carried out,
- 108 (18.3%) on referral to hospital,
- 58 (9.8%) answered 'other'.

The main time for the group responding 'other' was when they realised that their symptoms did not improve after they had visited their GP for the first time.

There was no statistically significant difference in sex when considering cancer before diagnosis. There was a statistically significant ($p<0.01$) difference between the proportion of cases in each age group and those considering a diagnosis of cancer. The younger age group were more likely than the older group to consider cancer before diagnosis. Those considering cancer before diagnosis are 141 (46.1%) in the younger age group and 279 (35.6%) in the older age group.

There was no statistically significant difference between the proportions considering cancer before diagnosis in the different deprivation groups (using both deprivation indices). There was a tendency for the more affluent group to consider cancer before diagnosis. The results of both indices are given in Table 60.

Table 60 Cases that considered a diagnosis of cancer and deprivation groups

Indices	Deprivation Groups		
	Group 1	Group 2	Group 3
Carstairs	163 (40.0)	363 (40.9)	69 (34.0)
SIMD	191 (41.5)	360 (39.3)	44 (36.1)

The 925 cases that did not consider cancer, were asked what they felt could be wrong. Of the 925 cases, 853 answered the question and table 61 shows the responses given.

Table 61 Reasons given for current symptoms

Reason for symptoms	Number 853	%
Don't Know	202	(23.7)
Piles	205	(24.0)
Inflammatory bowel disease	105	(12.3)
An infection	36	(4.2)
Ulcer	34	(4.0)
Polyps (not cancer)	31	(3.6)
Constipation	31	(3.6)
Gallbladder problems or Hernia	25	(2.9)
Ageing process	12	(1.4)
Appendicitis	10	(1.2)
An abscess	5	(0.6)
Indigestion	4	(0.5)
Other	153	(17.9)

This table shows that 24% of cases delayed in visiting a GP as they thought that piles caused their symptoms.

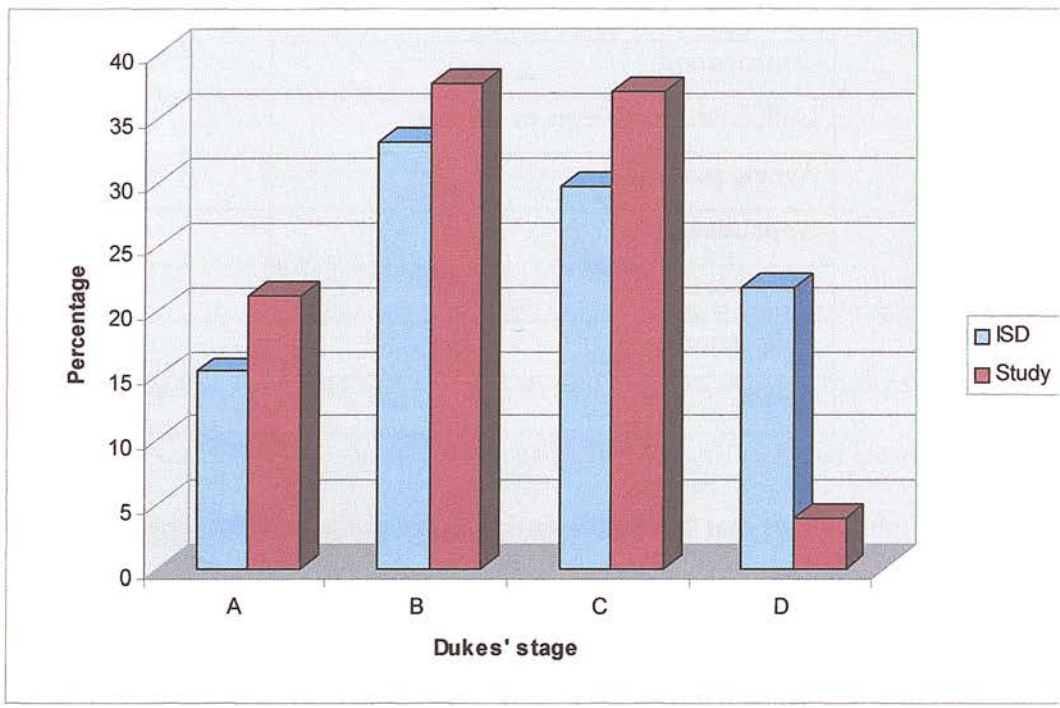
Analysis was carried out for all cases that did not consider they had cancer before diagnosis. The cases were classified into two groups; those thinking they had piles and those thinking other reasons for their symptoms.

There was a statistically ($p<0.05$) significant difference in the sexes and the proportions thinking they had piles and those thinking some other reason. Males were more likely than females to think they had piles. In the group thinking they had piles there were 71 (20.2%) females and 134 (26.7%) males.

Dukes' Staging

Figure 20 shows the Dukes' stage distribution from the latest available 24 months, as provided by ISD, from the Scottish colorectal cancer population and for 24 months recruitment to this study.

Figure 20 Distribution of Dukes' stage from ISD data and study cohort



The Dukes' stage data was available for 1188 cases, in 11 medical notes no Dukes' stage was recorded. Included in the numbers with Dukes' stage A are 20 cases that had a polypectomy and pathology results showed no need for further surgery. Included in the numbers with Dukes' stage D are 19 cases that had no surgery, due to advanced disease.

A further 14 rectal cancer cases had preoperative radiotherapy, which resulted in eradication of the tumour and no tumour material was available to stage at surgery and is shown as CH in figure 21. The distribution of Dukes' staging at diagnosis from this study is:

Dukes' stage A = **247**

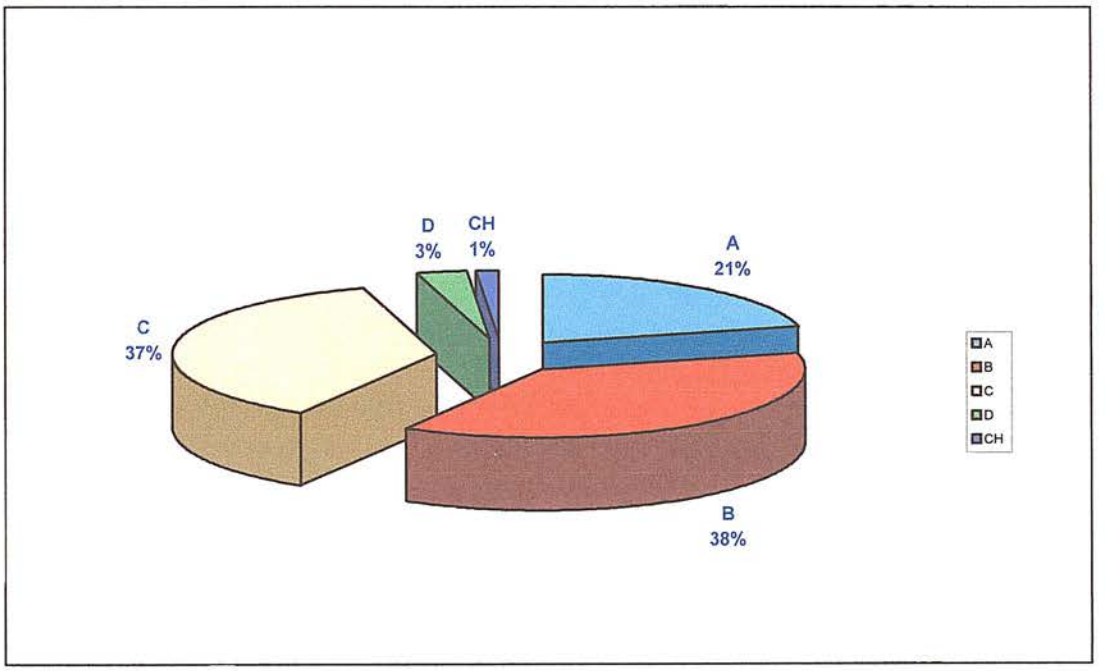
Dukes' stage B = **439**

Dukes' stage C = **432**

Dukes' stage D = **45**.

Percentages of the Dukes' stage can be seen in Figure 21.

Figure 21 Dukes' stage distribution for study cohort



Waiting time and Dukes' Staging

To identify if Dukes' staging was affected by waiting time, an analysis of waiting time with each symptom and each Dukes' stage was carried out. Table 62 shows the median waiting time and the 25th and 75th centiles by each Dukes' stage.

Table 62 Waiting times with symptoms by Dukes' stage

Symptoms & Dukes'	Dukes' stage											
	A 247			B 439			C 432			D 45		
Median & quartiles	25th	Median	75th	25th	Median	75th	25th	Median	75th	25th	Median	75th
Change in bowel habit	4.2	**13.0**	26.0	4.2	**13.0**	26.0	4.0	**8.7**	18.1	2.0	**8.7**	41.0
Rectal bleeding	1.2	**4.2**	17.4	2.0	**8.0**	17.4	1.85	**4.2**	21.7	2.0	**10.8**	52.1
Weight loss	8.7	**17.4**	26.0	8.6	**13.0**	26.0	6.0	**8.7**	25.7	8.0	**8.7**	26.0
Marked loss of energy	8.7	**13.0**	38	6.0	**13.0**	26.0	4.2	**13.0**	26.0	7.6	**10.7**	49.0
Wind & bloating	4.2	**8.7**	26.0	5.7	**13.0**	26.0	4.2	**12.4**	26.0	3.0	**8.7**	24.9
Loss of appetite	7.6	**8.7**	31.5	4.2	**8.7**	21.7	3.0	**8.0**	16.0	2.0	**4.2**	8.7
Mucus	3.0	**8.2**	28.2	4.2	**8.7**	26.0	3.7	**8.0**	17.3	7.0	**10.8**	62.0
Tenesmus	3.0	**8.2**	17.4	6.0	**13.0**	26.0	4.0	**8.7**	17.4	7.6	**13**	49.0
Abdominal discomfort	4.3	**13.0**	28.2	4.0	**8.7**	9.6	3.0	**4.2**	21.7	2.0	**4.0**	17.4
Pain	1.0	**4.2**	13.0	0.7	**3.0**	9.6	1.00	**4.0**	17.4	0.6	**1.0**	8.7
Nausea	6.4	**8.7**	19.5	0.4	**4.0**	13.0	0.4	**2.5**	11.9	1.0	**1.5**	7.0
Vomiting	0.21	**4.0**	17.2	0.2	**1.0**	6.5	0.1 -	**1.0**	13.0	1.0	**1.0**	2.0

Table 62 shows that the median wait time for Dukes' stage D with change in bowel habit, weight loss, marked loss of energy and abdominal discomfort are all shorter wait times than for Dukes' stage A.

However within the Dukes' stage D group the 75th centile wait time is much greater for change in bowel habit, rectal bleeding; marked loss of energy, mucus in stool and tenesmus than in the 75th centile for any of the other Dukes' stages for these symptoms.

Figure 22 shows the median waiting time in weeks, the 25th and 75th centiles for change in bowel habit, rectal bleeding and marked loss of energy.

Figure 22 *Median, 25th and 75th centile for wait time for with change in bowel habit, loss of energy and rectal bleeding*

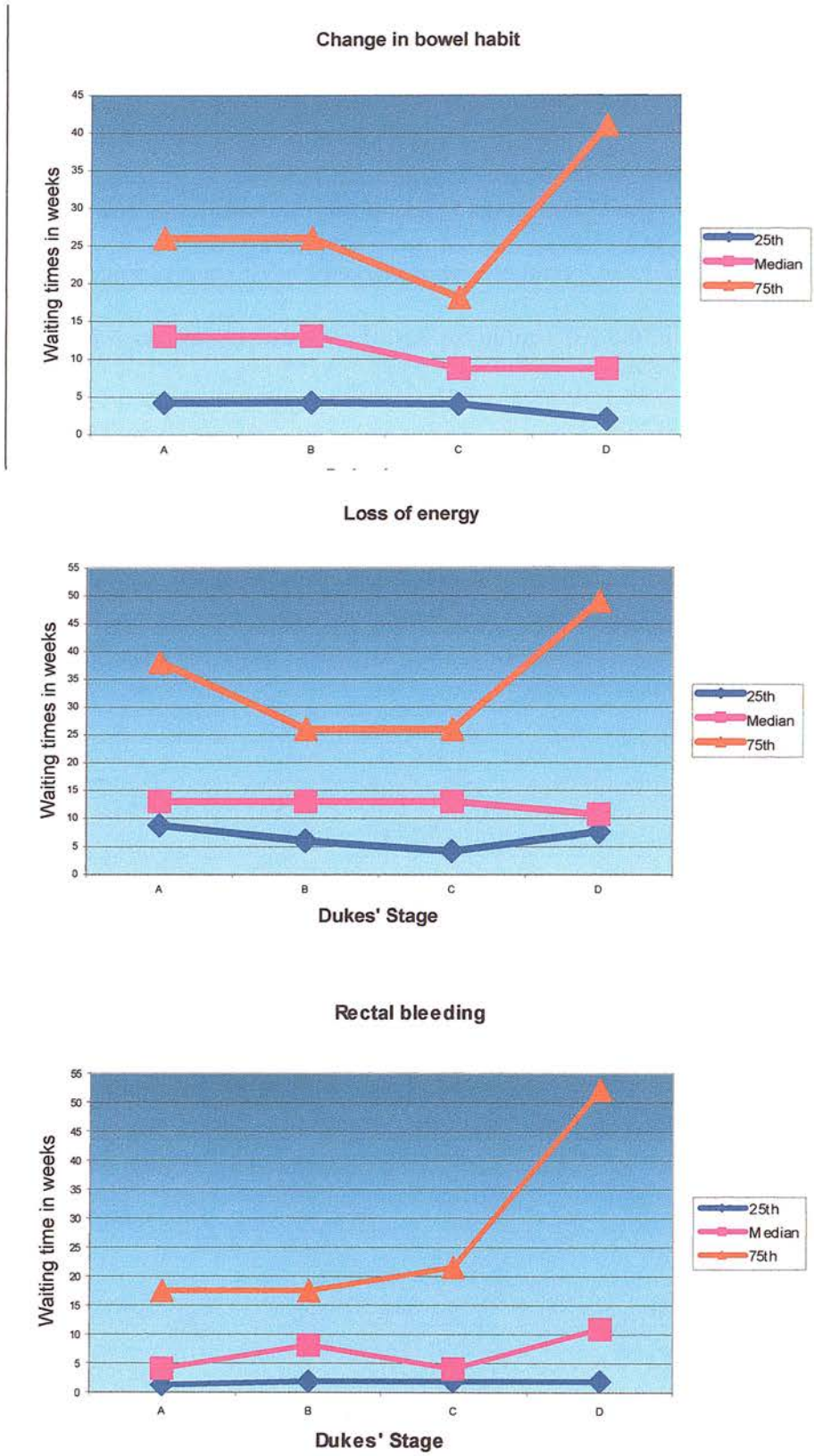


Table 63 shows the proportion of Dukes' stage for colon and rectal cancer

Table 63 Distribution of Dukes' stage and site of cancer

Site of cancer	Dukes' stage					
	A	B	C	D	CH[21]	N/A[22]
Colon	108 (15.7)	293 (42.5)	261 (37.8)	25 (3.6)	0	3 (0.4)
Rectum	135 (27.8)	144 (29.6)	167 (34.4)	18 (3.7)	14 (2.9)	8 (1.6)

Table 63 shows that the proportion of Dukes' stage A tumours in rectal cancer were greater than the proportion of Dukes' stage A tumours with for colon cancer in this cohort. There was a statistically significant difference ($p<0.001$) between the Dukes' stage at diagnosis and the site of cancer in the large bowel.

There was no statistically significant difference between sex, age groups, and deprivation groups, knowledge of colorectal cancer symptoms or perceived family history in the proportions with different Dukes' stage at diagnosis.

21 Cases with rectal cancer that have had pre operative radiotherapy and no residual tumour left for staging.

22 Cases that had no surgery and therefore staging is not available.

Rectal examination

Cases were asked if they had a rectal examination carried out at the first visit to their GP, 1311 gave a response. Rectal examination was carried out on 639 (48.7%) cases and 672 (51.3%) did not have rectal examination at the first appointment. The 672 cases that did not have a rectal examination at this first appointment were then asked if at any time before referral to hospital, they had a rectal examination by their GP. A further 97 (14.4%) did have a rectal examination before referral to hospital. Therefore, 736 (56%) of cases had a rectal examination at sometime before referral to hospital.

Of the 522 cases with rectal cancer, 442 answered the question on having a rectal examination at the first visit to a GP. Of these, 297 (67.3%) replied yes and 145 (32.7%) replied no to rectal examination at first visit to a GP. The 145 cases answering that no examination was carried out at first visit to GP were asked if they had a rectal examination at any time before referral to hospital. Of these, 138 cases replied, and a further 33 replied yes. Therefore a total of 330 (74.6%) of the 442 rectal cancers had a rectal examination before referral to hospital.

Analysing the 768 cases that presented with rectal bleeding to a GP, there was a statistically significant ($p<0.05$) difference between the proportions in the three age groups and those having a rectal examination at first visit to GP. In the younger age group 98 (56.6%) cases and 227 (69.8%) in the older age group had a rectal examination. There was a statistically significant difference ($p<0.05$) between the sexes and the proportions having a rectal examination at first visit to GP. Females were less likely than males to be given a rectal examination by their GP. In the group reporting rectal

bleeding 174 (60.8%) females and 280 (69.1%) males had a rectal examination at first visit to GP.

In the whole cohort, there was a statistically significant ($p<0.05$) difference between those with comorbidity and those without comorbidity and the proportion having a rectal examination at first visit to GP. Those cases with comorbidity were more likely to have a rectal examination at first visit to GP than those with no comorbidity. Of those with comorbidity 313 (52%) were given a rectal examination at first visit to a GP and those with no comorbidity 196 (45.8%) were given a rectal examination at first visit to GP. There was a statistically significant ($p<0.05$) difference between cases with no knowledge of colorectal cancer symptoms and some knowledge and the proportion having a rectal examination at first visit to GP. Those with 'some knowledge' of colorectal cancer symptoms were more likely to be given a rectal examination at first visit to GP than those with no knowledge. Those with some knowledge 315 (53.3%) were given a rectal examination at first visit to GP and those stating no knowledge of colorectal cancer symptoms 324 (44.9%) had a rectal examination at first visit to GP.

Referral letters

Referral letters were accessed from the medical notes and information on abdominal mass and rectal mass were extracted from the referral letter. Of 1212 medical notes accessed 204 (16.8%) cases had no referral letter or emergency admission letter in file and a further 89 (7.3%) cases were referred direct from the faecal occult blood testing study with no letter.

Information from the referral letter should indicate the level of urgency of the referral. Of the 919 with a referral letter 154 (16.7%) cases were referred as routine, 477 (51.9%) cases were referred as urgent and for 288 (31.3%) cases there was no indication given in the referral letter how the GP would like the referral to be treated.

Chapter 15

Referral Guidelines

Colorectal cancer referral guidelines

The Association of Coloproctology of Great Britain and Ireland (ACPGBI) (Thompson 2002) published a reference paper with the evidence to support the NHS 2000 guidelines for suspected colorectal cancer. The following analysis is a comparison of the data collected retrospectively from colorectal cancer patients and the data present by ACPGBI. The ACPBGBI data was primarily derived primarily from individuals referred to hospital for further investigations after presenting to GP with symptoms. This study cohort is individuals with colorectal cancer giving their symptoms retrospectively.

Table 64 and table 65[23] illustrate the evidence according to the site of the cancers.

Table 64 Rectal and sigmoid cancers and symptom criteria analysis

Criteria	Range within ACPGBI reviewed papers Meeting guideline criteria	Study population Meeting guideline criteria	CI (95%)
Both rectal bleeding and change in bowel habit	50-60%	39.2%	(35.8-42.8)
Rectal bleeding no anal symptoms	50-60%	49.6%	(45.9-53.3)
Rectal mass present on examination of rectal cancers	40-60%	11.4%	(9.4-13.9)
Palpable mass on left sided for sigmoid cancers	20%	N/A	N/A
Change in bowel habit is to looser and/or increased frequency	>90%	50%	(46.2-53.8)

23 Table 64 & 65 represent the range from published data meeting each criterion with guidelines and study population meeting guidelines.

Table 65 ***Caecal and Descending colon cancers and symptom criteria analysis***

Criteria	ACPGBI	Study population	CI (95%)
Present with iron deficiency anaemia	30 - 75%	27.9%	(23.4 - 33.0)
Haemoglobin level below 10g	54%	84%	
Present with abdominal mass	40 - 55%	9%	(6.6 - 2.1)
Present with intestinal obstruction	10 - 30%	9%	(6.6 - 2.1)

Tables 64 and 65 considered 1199 cases where the site of cancer was known.

The medical notes data collection tool in this study did not request the site of abdominal mass..

Low haemoglobin levels

The first haemoglobin level recorded in the hospital notes as close to the referral letter date or emergency admission date was used for this analysis. This information was available for 1212 cases. 161 (13.5%) cases were found to have haemoglobin levels below 10g/dl for women and below 11g/dl for males. There were 58 (36%) females with haemoglobin levels below 10g/dl (of these 10 were below the age of 50) and 103 (64%) males who met low haemoglobin level criteria.

The criterion for low haemoglobin levels does not consider those women under age 50 (50 considered the age of menopause) with a haemoglobin level below 10g/dl. In this cohort 10 females had a haemoglobin level below 10g/dl but were not included in the analysis for the low haemoglobin level criterion as the referral (NHS 2000) guidelines specify postmenopausal women.

Abdominal mass

In the 1212 medical notes reviewed 68 (5.6%) of GPs reported in their referral letter that a palpable abdominal mass was found. These 1212 case were asked 'did they have an abdominal examination'? those who said yes, were asked what the GP told them after the examination and 14 (1%), stated that they were informed by their GP that they had a lump or mass in their abdomen.

Rectal mass

In the 1212 medical notes reviewed, 5 (0.4%) GPs reported in the referral letter finding a rectal mass. However with further investigation of the referral letter in a further 88 cases the GP noted a suspicion of rectal cancer. A rectal mass was recorded or it was recorded that rectal cancer was suspected for 93 (18.5%) of all 502 rectal cancers cases. The data collected on rectal mass and abdominal mass was not considered reliable due to the small numbers of rectal mass and abdominal mass reported and the great difference in results when compared with the ACPGBI findings. There is also sample bias due to very few Duke's stage D cancers recruited to this study. This combination of events resulted in no comparison being carried out between the referral guidelines and this study cohort.

Chapter 16

Discussion

Discussion

This study is one of the largest population based studies of colorectal cancer which evaluates family history information in a systematic manner. Few population-based studies have reported on the proportion of colorectal cancer cases which meet modified Amsterdam family history (also referred to as HNPCC family history) criteria, even fewer such studies have reported on the proportion which meet criteria defined as moderately increased family history. No studies have published family history risk data on the Scottish colorectal cancer population in relation to family history.

The methodology used in this study also gave the opportunity to collect data on symptom presentation and waiting time with symptoms and to analyse these data with respect to deprivation and comorbidity. This the study also aimed to report on the proportion of individuals within this cohort that had symptoms meeting at least one of the high-risk criteria within the published guidelines for suspected colorectal cancer. The following outlines some of the main strengths and the limitations of the study.

Strengths

1. The study has a large sample size of individuals with colorectal cancer and family history; this was prospectively ascertained and has sufficient power to detect modest differences between groups defined by family history criteria.
2. The family history was taken and the pedigree drawn by a trained research nurse in a face-to- face interview. Information on at least three generations was recorded and universal nomenclature was used in the drawing of the pedigree.

This is equivalent to the level of family history recording in a clinical cancer genetic setting.

3. The methodology was found to be highly acceptable to participants. This was confirmed by the results of a small acceptability sub-study. A short report of this study can be found in *Appendix 13*.

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Limitations

1. The methodology of the study resulted in the cohort being biased by the small number with Dukes' D stage cancers participating. However this bias in this cohort is not expected to affect the family history analysis with respect to assigned family history risk. However the sample will be biased regarding referral to cancer genetic services.
2. Access to medical notes was found to be problematic resulting in 21% of medical notes being unavailable. These problems arose from access by research staff to medical records departments and medial notes not actually being in the medical records department once access had been granted.
3. The data collected from referral letters within medical notes was found to be incomplete. There was lack of symptom detail and examinations carried out by GPs recorded in referral letters.
4. Although the number of primary research questions (related to the influence of family history) was limited I did carry out multiple statistical tests investigating other aspects of the data. These analyses were exploratory and results cannot be considered robust since multiple testing was performed.

5. The analysis has shown that the results can only be generalised to white Caucasians due to the high percentage within this cohort and the few cases from other ethnic groups.
6. Data presented in this thesis are a case cohort and no control data has been reported.

Changes to study

The changes that the author would make to this study if it was to be repeated:

1. Would aim to recruit research nurses on a seconded basis, and in particular, those working within areas where colorectal cancer cases are cared for. This would possibly increase ascertainment figures.
2. Set up access to audit and medical records departments prior to recruitment of cases.
3. Establish a more robust system to collect reason for cases not participating in study.
4. Request ethical approval to contact cases sent a high and moderate risk letter to follow up, if they or their family had activated a referral to genetics department. If they had attended a genetic department seek consent to access this final risk.
5. More research nurses may have increased ascertainment and recruitment.

Ascertainment and recruitment of cases

This study was conducted within the SOCCS study that recruited people throughout Scotland with colorectal cancer. In a 24 months data collection period, 3761 individuals were identified.

The Information Statistic Division of Scottish Cancer Registry (ISD 2003) publishes incidence figures for colorectal cancers in Scotland. Data for 1997 were available at start of this study. For the age group 16-79, 2566 cases were registered with ISD. Therefore, approximately 5132 cases could be anticipated during the 24 months of data collection.

At the time of writing, colorectal cancer registrations were available for the year 2000. The data presented in the result section for ascertainment related to the year 2000 published data. There were 2726 cases in the target age group, an absolute increase of 160 cases compared with 1997. Ascertainment of cases in the study was therefore between 69% and 73% of that expected throughout Scotland.

The Scottish Cancer registry data has been found to have high levels of accuracy and completeness (Brewster et al 1994, Brewster et al 2002)

During this study there was a reorganisation of colorectal cancer services by which several hospitals changed admission for surgery to feed into nearest city hospital with the aim of developing centres of excellence. We found ascertainment in hospitals to range from 45% to 134% (see table 33) of the numbers expected based upon published colorectal cancer registrations for 1999. This reorganisation of services may explain why ascertainment figures from some hospitals were greater than expected. Alternatively, these increased figures may reflect an accurate ascertainment with increasing numbers diagnosed with colorectal cancers in that hospital.

Reasons for lower ascertainment and recruitment to the study may have been due to the following:

- We relied on the colorectal cancer nurse specialist (CCNS) in hospitals to identify patients eligible for the study. The CCNS would then give the patient information about the study. The patient would inform the CCNS (if still in hospital) whether they would like to be contacted by the research nurse for recruitment. In some hospitals the CCNS was not informed of all cases of colorectal cancer, thus lowering the likelihood of accurate ascertainment.
- In hospitals with no CCNS, ascertainment of eligible patients relied on the surgical ward staff informing the research nurse of eligible patients. A lack of continuity in staff led to sub-optimal referral of eligible patients despite educational input and operating protocols that were discussed and agreed with ward staff. The ascertainment in these hospitals was lower than expected.
- Ascertainment was also pursued through audit data in most hospitals. However, in most audit departments there is a substantial delay in entering data. This resulted in the research nurse identifying eligible cases many months after their diagnosis. These cases were sent a letter with information about the study by the Consultant surgeon or CCNS (if they felt it was appropriate). Recruitment in cases approached by this method was lower, possibly due to late ascertainment.
- A confirmed diagnosis of colorectal cancer was required for recruitment to the study. The timing of the approach and the age of patient at diagnosis may have been important. The decision to take part in a research study soon after diagnosis may be affected by age. There was a difference between the age groups (16-54, 55-64 and 65-79) and the proportion of non-participants and

the participants. Of the non-participants 7.1% were in the younger age group and 70% in the older age group compared to those participating where 20.1% were in younger age group and 51.3% in older age group. In this study, older cases were less likely to participate.

- Socioeconomic status may play a role in decision making to take part in any research study. There was a high level of non-participation in the Greater Glasgow Health Board area in the study. This area is highly populated and has a higher proportion of the most deprived group (ISD 2003). It has been found by other studies that socioeconomic status was a predictor of participation in research studies. McCaffery et al (2002) found a low recruitment rate of the more deprived group in Greater Glasgow in a study of individuals being offered sigmoidoscopy surveillance.
- It is possible that employment of more research nurses would have increased the ascertainment and recruitment. It was demonstrated in the study that if a nurse only recruited from one hospital and/or was known staff member ascertainment and recruitment were higher compared to a research nurse who had to ascertain and recruit cases from several hospitals. The staffing for the study employed the equivalent of 5.5 full time nurses to ascertain and recruit cases and in addition also to recruit controls and many unaffected first degree relatives.
- As ascertainment to the study was exclusively through surgical teams individuals with polyp cancer, treated by endoscopy alone, were picked up on audit data and therefore approached several months post treatment. This is likely to have reduced participation in the study.

Ascertainment and recruitment was affected by the time it took for each hospital to become confident with the study procedures and to build a working relationship with the research nurse designated to their hospital. Of the 1540 cases, 597 (38.8%) were recruited in the first year and 943 (61.2%) in the second year of the study. This may reflect an increase in the confidence of the CCNS and other nurses in the designated research nurse. This fact underscored the importance of retaining staff for the duration of the study.

In hospitals with a CCNS the ascertainment was usually 75% and above, but elsewhere it was generally well below 75%. In three hospitals with no CCNS, ascertainment was above 75%, however in these hospitals the research nurse was also a part time member of staff or on secondment to the study from that hospital. This would suggest that the ward staff were more confident in communicating with their own colleagues about the study than to a research nurse previously unknown to them.

Alternative study methodologies may have led to increased ascertainment and recruitment. The use of audit in a Scottish study of this type would rely on every hospital collecting the same dataset and this is currently not fully operational in Scotland.

Alternatively, individuals presenting to an outpatients department with lower gastrointestinal symptoms may offer the prospect of increased recruitment. A major disadvantage of recruiting individuals in this way is that they require to be followed through to diagnosis and the majority of these cases will not have colorectal cancer. This may be a more feasible methodology in a study of a single hospital. Another

disadvantage of using this alternative methodology is that a family history would be taken for all recruited cases, many not with colorectal cancer. Taking family history in this manner is likely to identify individuals with a family history of breast and ovarian cancer as well as family histories with colorectal cancer.

Future population studies of colorectal cancer in Scotland might be able to make better use of audit data and pathology databases to ensure high levels of case ascertainment. Once these systems are well established nationally, careful attention must be paid to ethical and data protection guidelines.

In view of the higher ascertainment and recruitment where the research nurse was known to hospital staff, future research studies may want to locate the research nurse within the nursing team. This may be a seconded member of staff or a new member, integrated into the surgical team. In Scotland this model has been proposed for both breast and colorectal cancer through the National Translational Cancer Research Network (NTRAC). In this model, one research nurse will have responsibility to make contact with each eligible case. Following consent they will collect a core dataset and inform patients about other research projects for which they are eligible and could consider participation.

In the past nurses have tried to protect their patients from research studies. Poor professional development may have led to an individual's lack of research knowledge, which may be shown in a lack of enthusiasm and interaction with research studies. Recently there has been a drive by the Scottish Executive to widen nurses' knowledge of research methodology, data collection and to involve more nurses in research planning

and development. This study was active before the Scottish Executive initiative was fully implemented. Ascertainment could have been affected by the lack of research knowledge in some hospitals. This was most evident in the early stages of developing the recruitment process when some ward nurses refused to inform the research nurse of cases eligible for the study.

The role of CCNS in Scotland evolved with little strategic direction. Each post developed differently with the result that each CCNS post has a wide range of different skills and responsibilities. Only recently work has begun to assign core competencies for these posts both in terms of skills and academic requirements. The role of interacting with research studies within hospitals has been devolved to CCNS in each area. However, many of the CCNS post do not have a nurse with the academic knowledge to fully understand the implications for a research study of incomplete data.

It was stressed by several CCNS in the study that the time at which cases were approached with study information appeared to be important. The study tried to acknowledge this with guidance from the CCNS and allowed them to give out the information about the study. Despite this approach many older cases chose not to take part and eligible patients approached some months after diagnosis had lower recruitment rates.

It is possible that the older generation are still suspicious of research studies and choose not to take part. Cases that have their diagnosis and treatment complete before being approached with study information may not want to think of themselves as someone with colorectal cancer.

The study was conducted within a larger study and it may have been that this adversely impacted on recruitment since the larger study involved collecting a blood sample and gathering additional information. It is also likely that smaller studies within single hospitals may be able to achieve higher ascertainment and recruitment rates. In a population based colorectal cancer study by Katballe et al (2001) the recruitment rate was 1200 (80%) of 1514 ascertained, this study only collected family history information and did so via the patient's own surgeon. A French Population based colorectal cancer study collected more detailed information including family history and blood samples and reported their recruitment as 767 (56.8%) of 1351 cases ascertained (Audrieu et al 2003). A Southern Californian study reported recruitment of 1431 (57%) from 2489 cases ascertained (Peel et al 2000). These two studies compared more favourably with the 41% recruitment of those ascertained in this study. Both of these studies ascertained their cases from a pathology database.

Participants

A large cohort of 1540 participants was recruited to this study (41% of all eligible patients). This study is the largest UK and possibly European, prospective cohort of colorectal cancer that has data on (three-generation) family history. Three other large colorectal cancer cohorts have been published. Katballe et al (2001) from a cohort of 1200 cases collected family history information on first-degree relatives of cases and second-degree relatives if the case was under age 50 at diagnosis. Audrieu et al (2003) and Peel et al (2000) collected information on all first and second-degree relatives.

Analysing the distribution of participating cases by Health Board, it was found that a higher number of cases were recruited from large city hospitals. This was expected as

many Scottish city hospitals are establishing centres of excellence for colorectal cancer care. Many of the recruited cases were diagnosed at district hospitals but had their surgery in a city hospital. Larger hospitals in Glasgow were an exception, with relatively fewer participants recruited.

Comparing the non-participant group with the participants the median age of the participants in the study was 65 years, whilst that of the non-participant group was 70 years.

The 1999 published data for Scottish colorectal cancer registration in the age group 16-79 reported the male: female ratio as 55.4% males and 44.6% females (ISD 2003) which is similar to the 58.5% males and 41.5% females in this study cohort.

There were 309 (20.1%) cases in this study under age 55 at diagnosis; other published studies report lower proportions in this age group. Higher participation in this study may be due to cases under age 55 being offered mutation analysis for three mismatch repair genes regardless of family history risk. Those over age 55 years were not offered any form of gene testing.

Conclusion

This study recruited a large prospective population-based cohort of cases with colorectal cancer with detailed family history information. There is a small age bias in the cohort, participants being marginally younger than the non-participants and there was a small difference in the proportions of males and females compared to the latest published colorectal cancer data. There is a bias in the study as the proportion of cases with more

advanced disease (by Dukes' stage) was lower than expected. However these biases are unlikely to have a major effect on the results of the main research questions related to family history with the exception of generalisability of the results due to the cohort being almost exclusively white Caucasian.

Non-participants

Limited data are available for the cases not recruited to the study due to restrictions placed on data collection for ethical reasons. A total of 2079 cases identified with colorectal cancer did not participate in the study. The non-participants fall into two distinct groups: those 'unable to take part,' 856 (41%) cases and those that 'did not want to take part,' 1223 (59%) cases. All information collected on the non-participants was within the ethical approval guidelines.

Non Participant data is extremely important to any study. This data will be combined with the recruitment data and will complete the overall ascertainment figures. This data is also equally important in order to ascertain any bias within the study.

'Unable to take part' group

Cases recorded as 'unable to take part' were never given information about the study to enable them to choose whether to take part. The CCNS and some Consultant surgeons (CS) made the decision whether, and at what stage, an eligible case would be given information about the study. Many CCNS would only give information on age and sex of eligible patients as they felt that the research study had no need to know more information on non-participants. This reluctance to give more information resulted in a large number of cases with limited data.

The proportion of those 'unable to take part' in relation to the numbers ascertained varied greatly between Health Boards. This ranged from 9% in Shetland to 30.8% in Lanarkshire. These cases were never informed of the study and the differences are likely to be due to the subjective nature of decisions made by each nurse responsible for giving information to patients about the study. This decision is likely to be based on a number of factors such as years of practice at a senior level, the depth of research knowledge, workload pressures, their personal views on research studies, and personal feelings on other professionals interacting with their patients. This information is important to be aware of the bias that could be introduced to the study.

'Did not want to take part'

Cases recorded as 'did not want to take part' were given information about the study and chose not to participate. The ascertainment protocol in the majority of hospitals stated that the CCNS would give the study information pack to eligible patients.

There were several methods for the research nurse to know whether a case wished to be recruited to the study. It was very common for the patient to inform the CCNS whether or not they wished to take part and this information was passed on to the research nurse by the CCNS. On some occasions the case would return the patient reply form given in the information pack, indicating that they did not wish to take part and no further information was given or requested. Other eligible patients agreed that the research nurse could contact them but then told the research nurse that they did not wish to take part, in some instances the cases volunteered the reason. Other eligible patients that had been given an invitation failed to reply.

The proportion of cases not wanting to take part ranged from 13.9% in Borders to 63.6% in Shetland. In larger Health Boards it ranged from 28.3% in Grampian to 39.5% in Argyll and Clyde (see table 28).

There was no difference in sex or age distribution between those that 'did not want to take part' and those 'unable to take part'. In the group 'did not want to take part' more information was available on whether surgery was performed and the type of surgery performed than for the group 'unable to take part'.

When surgery information was available, a higher proportion in the 'did not want to take part' group had curative surgery performed. These results appear to show that the patients 'unable to take part' were more ill at diagnosis than those choosing not to take part.

Information that was collected on non-participants included; sex, age, Health Board area, was surgery performed and was it curative or palliative and the reason that the case was unable to take part. It is not possible to compare the socioeconomic status of those not participating in the study. The ethical committee ruled that individual postcodes may enable identification of patients, so should not be recorded for non-participants. The only information available that would indicate any measure of socioeconomic status was the Health Board area. In both non-participant groups a higher proportion were in the Greater Glasgow Health Board area (which has a high proportion of deprived individuals) than in others.

Of the eligible patients identified for the study, 57% did not consent for a variety of reasons. A more robust methodology for collecting reasons for non-participation may

have yielded data that would be valuable in the design of future research studies. Possibly if the CCNS were given a non-participant sheet to complete (containing a choice of reasons for being unable to take part) more data on non-participants may have been gathered. However, asking them to complete a sheet and return to the office would have added to their workload.

The methodology used by Katballe et al (2001), Audrieu et al (2003) and Peel et al (2000) to collect data from pathology databases and write to the eligible cases resulted in a higher recruitment than this study suggesting that the decision by the nurses not to give the information to certain individuals and excluded some cases that would have chosen to take part.

Conclusion

A substantial proportion of cases did not consent to the study that resulted in recruitment bias. There was a small age bias as a higher proportion of older cases did not participate and, from the data provided, a higher proportion of the more ill patients did not participate.

Data collection

Family history

Family history was requested at recruitment and of the 1540 cases participating in the study, 31 (2%) were unable or refused to give family history information.

The data included all family members over a minimum of three generations. Pedigrees were constructed and recorded on a standard family history form (*Appendix 9*) to the

quality expected within a clinical genetic setting, using universally recognised nomenclature (Bennett et al 1995).

Other large studies have used questionnaires or a combination of questionnaire and telephone interview to collect family history data. These methodologies have been used successfully by many studies that collect only first and second-degree relative information. However, to collect the more in-depth family details necessary for this study the use of a family history questionnaire would require a very complex form.

There is little published evidence on the most accurate method of taking a family history. However, clinical genetics services throughout the UK continue to take and record family history in a face-to-face interview believing this to be the best available method.

Other studies collecting family history information from colorectal cancer cases did so with the aim of investigating the accuracy of the family history data given not to assess risk. In many cases this was felt to be most accurate for first-degree relatives and slightly less for second-degree relatives (Love et al 1985, Douglas et al 1999, Simons et al 2000). However, Mitchell et al (2004) found a much lower degree of accuracy. The family history in that study was taken and recorded by a genetic nurse but the data were collected many years before publication and it may be that understanding of family history of colorectal cancer as a risk factor was much less advanced, or was not discussed within families at that time. Alternatively it may be that discussing cancer within families was still taboo or it was still common for individuals not to be informed of their cancer status.

In this study I did not aim to assess the accuracy of the family history, but to assess GP knowledge of family history in relation to published guidelines and to assess the extent to which GPs had also identified family history risk. Therefore, family history reported by the cases at recruitment was that to which a risk was assigned following Scottish criteria. No attempt was made to confirm cancer diagnoses in relatives. This is the same method GPs could apply to assess risk. I also aimed to assess if individuals with colorectal cancer perceived a family history risk.

Incidentally, within the study, there was a crude way of assessing the quality of family history given by each case. As part of the larger study, siblings and/or parents of the cases were recruited into a parallel study. The baseline was the original family history taken from the case and with consent from the case it was extended by any further information from the family. Each family history was then reassessed. After interviewing 309 relatives, new information was often added, but only two families showed a change in risk category from low to moderate risk, and only one family from moderate to high risk. In no instance was the risk reduced. It appears that the family history given initially by cases was as accurate as the information known within the family. However, this sample may be biased towards those families that speak to each other and enjoy a close relationship.

The family history information in this study was collected at recruitment and there was a mean recruitment time of 21 weeks from diagnosis until recruitment. We asked what information the case was aware of at time of recruitment. The information sheet indicates that we will ask information on family history and when the case was contacted to arrange a home visit this was discussed again. Each case had the same

opportunity to seek out family history information and to discuss it with GP or other health professional before recruitment.

The study collected data to assess if high or moderate family history was identified by the GP. Data discussed later in this thesis clearly illustrate that many cases with knowledge of cancer in their family did not discuss this with their GP and that the GP does not routinely ask information on family history to assess risk.

Conclusion

No other published study with a large population based cohort has collected such detailed data on family history collected in a systematic manner. Mitchell et al (2004) used a similar methodology in a relatively small sample.

Family history information in this study was gathered to inform risk assessment using published Scottish guidelines and to assess the number and proportion of cases with a family history requiring referral to cancer genetic services. The recruitment biases reported above in this cohort should not affect the validity of these results.

Symptom data

Data on symptoms experienced prior to reporting to a GP were collected from cases through a structured symptom interview. This method carries a number of advantages:

- It is an effective way of ensuring a response when collecting data from a large number of individuals over a wide geographical area, as data are recorded at the meeting and no postal return is required.
- Asking a set of predetermined, precise questions in the same way and in the same order can increase the reliability of the data.

- As the research nurse is present to clarify and assist with the meaning of the questions, the responses are likely to be more valid.
- There is the assurance that data are given by the case, which cannot always be guaranteed with self-completed postal questionnaires.
- This methodology can overcome literacy problems that may be experienced by the case, reducing the bias of the sample.

Although not an advantage over postal questionnaires, carrying out the interview in the privacy of someone's own home reduces the fear of others overhearing personal responses. One disadvantage with regard to an administered structured interview is that the researcher may not elicit the true answer that is willingly divulged to a self-administered questionnaire.

Data from medical notes

Of the 1540 cases recruited to this study, the medical notes were accessed for 1212 cases by June 2004. The process of accessing medical notes was very bureaucratic and caused significant time delays in many hospitals, particularly in the West of Scotland. Many medical records departments insisted that a request letter was sent to either the medical director or the Caldecott guardian and a reply received before re-contacting the medical records department. On many occasions, the medical director or the Caldecott guardian was the same person that had signed the trust management approval letter for the study, but medical records managers would not give access to records until this procedure was followed. Access could have been simplified if the trust management team giving approval for the study had notified all the departments likely to be involved with the study. Alternatively, as the Research and Development departments are credited with

the study as research activity within their hospital they could be the co-ordinators with departments to gain permission to access the data required with consent forms.

Once procedures were in place for accessing medical notes, further problems were encountered with their availability. It was often found that medical records staff were not available to have notes accessible or the notes were in the hospital system and not in the records department.

On some occasions the staffing problem was solved by payment for notes to be made available. The problem encountered with unavailable medical notes was more difficult to resolve and in order to circumvent it; notes were requested 3 months after recruitment. It was thought that notes would be more available three months after discharge than before the first outpatient appointment, normally at six weeks. However this was not found to be the case. The lag time in requesting notes was reduced to one month and produced similar results to waiting 3 months.

A total of 328 notes were unavailable at first request. This may be the result of internal audit on colorectal cancer patients or many simply reflect the fact that some hospitals take longer to return medical notes to medical records departments. The Research and Development department should inform research studies of current audits, if data collection relies on access to medical notes. An example of good practice was found in two hospitals, where a medical records officer was responsible for all notes being available to both research and audit projects. In these hospitals 96% of notes were available when requested for the first time. This compares to the situation in the hospital with the highest deprivation only 9% of notes were available at first request.

Other studies using medical notes to access required data have acknowledged that they had a degree of difficulty. This resulted in a number of individuals recruited to their studies having incomplete data (Aitken et al 1995, Douglas et al 1999) as was experienced in this study.

Conclusion

Although 21% of the medical notes were not accessed for data collection there was no difference in the age, sex or deprivation categories that would result in bias of the cohort for analysis using medical note data.

The medical notes when available are an excellent source of objective data. In this study these data included information on haemoglobin levels (as laboratory results were clearly documented and dated). In most, but not all hospitals, Dukes' stage and the Tumour Nodes and Metastatic (TNM) status was recorded on pathology form or in a minimum dataset form. This study also required data from the GP or doctor's referral letter, these data on symptoms at presentation and examinations performed by GP were found to be less reliable and on many occasions not available. Future studies requiring these data should consider employing the use of a standard referral form by GPs for data capture.

Deprivation Indices

The deprivation index used by the ISD on Scottish population and colorectal cancer data is the Carstairs index. The latest data published on deprivation and the Scottish population are for the year 2001 and report on all ages. These data show that 25.8% of Scottish individuals are in the most affluent group (as defined in this study). In the colorectal cancer population in the year 2000 and in age group 16-79, 22.3% were in the

most affluent group; compared to 27.1% in this study. Similarly the proportions in the most deprived group are 15.2% in the Scottish population, 14.9% in the colorectal cancer population and 13.6% in this study.

The incidence of colorectal cancer has been increasing more rapidly among the more affluent group in Scotland resulting in a widening of the "deprivation gap" between the most affluent and the most deprived groups. Therefore, the increased percentage in the most affluent group in the study may be an accurate representation of the current colorectal cancer population. However, this cannot be confirmed until the data for the years 2002 and 2003 are available.

The Scottish Index of Multiple Deprivation (SIMD) has only been published recently and was the second deprivation index used (a detailed discussion of the Carstairs and SIMD indices are presented in the methods section). The deprivation groups in this index were more difficult to compile but followed a similar method to that employed in forming groups defined by the Carstairs index. The distribution was 29.5% in the most affluent group and 11.5% in the most deprived group. It was not possible to compare deprivation between the Scottish population and the colorectal cancer population, as no data have been published using the SIMD index.

Indices used in the study are derived from different datasets. The SIMD index data are derived from multiple sources of live data and it aims to be a dynamic source of data. The Carstairs index is created from the latest census data that is only updated every 10 years. The Carstairs index is often criticised in the literature for being out of date by the time the census data are available. Most analysis carried out involved an investigation on

the effect of deprivation and both indices where used. In all of the analyses the results were similar.

Conclusion

The Scottish Executive identified inequalities in various aspects of health and has invested in numerous projects that will generate more detailed information on the reasons for inequalities in health and areas of inequalities that could inform public health campaigns.

Published data from ISD show that in Scotland the incidence of colon and rectal cancer is greater in the most affluent groups and the deprivation gradient is steeper in those diagnosed with colon cancer. There is little difference between the deprivation groups and mortality. However there is an inverse survival (especially in rectal cancer) among most affluent groups (ISD 2003). In this study there was little to suggest that the most affluent group are treated any differently from the most deprived group by GPs or that the groups differ greatly in behaviour when lower gastrointestinal symptoms are present. We found no differences in waiting time with symptoms, taking medication for symptoms, discussing symptoms with other people, or in the number of visits before referral for investigations. These findings were robust to method of categorising the deprivation groups.

The Carstairs index is considered by some not to be an accurate measure of deprivation due to the limited measures of deprivation used to comprise the total score. The SIMD index used more current and possibly more accurate data for assessing deprivation status but in this study it gave similar results to the Carstairs score. This means that both

indices using different datasets arrived at comparable total scores. The new SIMD index allows more specific areas of deprivation to be included and an advantage of this index may be seen in studies wishing to investigate specific aspects of deprivation.

Comorbidity

Comorbidity data were collected from medical notes. The data collection tool used was the Charlson index (Charlson et al 1987), one of the most commonly used in UK research. We investigated if there was any association with comorbidity and delay in presenting with symptoms. We postulate that those cases with greater comorbidity might be more frequent visitors to the GP and might either report new symptoms of any kind more quickly or alternatively that they may delay in reporting as they have other more serious symptoms of other conditions. Cases with higher levels of comorbidity may not visit their GP as since often as they are maintained on medication for chronic conditions by repeat prescriptions and any new symptom may be interpreted as an effect of medication.

Comorbidity data in this cohort were available for 1208 cases and analysis of these data has shown that 505 (41.8%) cases had no comorbidity at the time of diagnosis of colorectal cancer. A further 342 (28.3%) cases had one comorbid condition and 361 (29.1%) cases had more than one comorbid condition. The number of cases in the study with comorbidity scored by Charlson index was much higher than that reported in a thesis by Stockton (2001). Stockton found only 15% of colorectal cancer in Scotland at the time of diagnosis to have any comorbidity at diagnosis using the Charlson index. The reason for this large deficit cannot be easily understood since information was not available on how the Charlson index was scored.

The information we have available on the non-participants suggests that patients with more comorbidity were more likely to be excluded from the study by the CCNS. In addition, individuals with more comorbidity may present with a poorer prognosis than those consenting to the study, although data to explore this are not available. It had been previously found that cases with higher levels of comorbidity are excluded from oncology research projects (Schag et al 1994) and it is reasonable to believe that this also happened in this study.

Dukes' stage of tumour

Dukes' stage in colorectal cancer identifies the severity of disease at diagnosis. Analysis carried out using Dukes' stage and total number of comorbid conditions did not show any statistically significant difference between Dukes' stage and number of comorbid conditions at diagnosis.

There is little literature on the relationship between comorbidity in colorectal cancer and delay in presenting with symptoms. Porta (1996) did find that cases with colorectal cancer and comorbidity did present sooner with symptoms than those with no comorbidity, but this was a small sample of 110 cases.

Analysis of the study data did not show any association with delay in presentation with symptoms and the number of comorbid conditions present at diagnosis (resulting in no difference in median waiting time for those with or without comorbidity). The results from this study would suggest that comorbidity status at diagnosis of colorectal cancer has little association with the presentation of symptoms or Dukes' stage at presentation.

This result should be interpreted with caution for those diagnosed with Dukes' stage D, as the sample of cases in this category was relatively small.

Data for all ages were available from ISD for Dukes' stage for cases registered in the year 2000 and 2001. Comparing these data to the 24 months study data there is a clear deficit of cases with Dukes' stage D in the study population.

Conclusion

Comorbidity was not associated with delay in presenting with symptoms or with the Dukes' stage at diagnosis. However, the cohort consisted of relatively few cases with Dukes' D stage tumours that may affect our power to detect such differences.

Family history of colorectal cancer

Until recently family history had been overlooked as an important risk factor in colorectal cancer. However in the past few years in Scotland, Scottish cancer genetics recommendations have recognised the importance of evaluating a family history of cancer and have drawn up appropriate clinical guidelines.

In 1995 the Department of published a report on, 'The advances in the genetics of common diseases, the implications for the NHS'.

This report stated:

> *"If the potential benefits of this progress are to be achieved a carefully planned programme of research and development will need to be implemented, with service organisation and development involving ongoing formal evaluations and integration of primary care into genetic services"*

Demand for cancer genetic services has increased since this time. However this increase in demand has primarily been from those individuals with a family history of breast

cancer (Wonderling et al 2001). The ongoing National breast screening programme for women age 50 and over may have led to a higher public recognition of the availability of breast cancer surveillance. The knowledge that a family history of breast cancer increased the risk of breast cancer may have driven a demand among women younger than age 50 for breast surveillance.

Due to regular breast awareness campaigns, many women realise when they reach 50 year of age they should attend for regular mammography through a surveillance programme. Many women will have experience of female relatives attending the surveillance programme and have relatives and/or friends with a diagnosis of breast cancer.

Breast cancer has a high public profile and has enjoyed the benefits of media attention through regular public health campaigns, abundance of public targeted information leaflets, breast cancer awareness month and women's journals regularly featuring breast cancer and more recently family history of breast cancer.

Colorectal cancer has no National surveillance programme equal to the breast surveillance programme. Colorectal cancer is not so widely publicised or bowel habits discussed publicly unlike the symptoms of breast cancer. The stigma of having a colostomy following a diagnosis of colorectal cancer has made colorectal cancer less socially accepted (MacDonald & Anderson 1984). In recent years there have been changes in surgery and treatment that have lessened the need for permanent colostomy. There has been limited research carried out on family history in patients with colorectal cancer. The evidence in support of recommended management strategies for individuals

with a family history meeting modified Amsterdam criteria (also known as high risk family history or HNPCC family history) is from observation studies and not randomised trials in families with high numbers of cancer cases. The available evidence suggests that surveillance management can prevent a colorectal cancer. However larger National or international studies are required to provide more robust evidence. The evidence for management of cases with a lesser degree of family history is not evidence based and is based on consensus of expert opinion.

Scottish guidelines for family history risk assessment

Scottish guidelines[24] for those with a family history of colorectal cancer have been developed and implemented. These recommend an assessment of family history with an individual level of risk that would give recommendations on the timing and frequency of surveillance that is offered to the individual. The levels of risk and the thresholds for surveillance recommended by the Scottish guidelines have varying degrees of evidence for their development and implementation, as noted above.

This study reports the proportion of cases with colorectal cancer that have a high or moderate family history. However, it is not possible to discuss such cases in isolation from their first-degree relatives. When a case meets the criteria for high or moderate risk due to family history they are informed that all first-degree relatives (age dependent) are 'at risk' and will be eligible to enter a surveillance programme to prevent colorectal cancer.

The criteria used to assign a high-risk to a family history in Scotland are the modified Amsterdam criteria, (which are used internationally to identify families that should be offered mismatch repair gene mutation analysis). These criteria were developed at a consensus conference hosted in Amsterdam by the International Collaborative Group on Hereditary Non Polyposis Colorectal Cancer (ICG-HNPCC) (Vasen et al 1999). They are applied Internationally, including the UK, to assign a high-risk to a family history of colorectal cancer.

24 Scottish guidelines are criteria for assignment of family history risk and surveillance recommendations. The risk assignment is detailed as high, moderate and low risk.

Patients with a family history that does not meet the high-risk criteria are assessed for a lower criterion that categorises them as having a moderate risk family history. This categorisation has a less firm evidence-base than the modified Amsterdam criteria. A UK consensus for moderate risk criteria for family history has not yet been reached within cancer genetic services. There is little published literature to provide the evidence required for efficacy of surveillance, the optimum number of screens required and the criteria to assess family history into this moderate risk group. Each cancer genetic service outwith Scotland varies slightly in moderate risk criteria, and the recommended surveillance informed by the risk criteria also varies.

The lifetime risk in Scotland of developing colorectal cancer is 1 in 16 for males and 1 in 20 for females (ISD 2004).

There are two Scottish family history critera for a moderate risk of developing colorectal cancer:

- One first degree relative with colorectal cancer under age 45 at diagnosis,
- Two first degree relatives with colorectal cancer, one diagnosed under the age of 55.

These criteria would equate to an approximate lifetime risk of 1 in 4, for a person meeting this family history criteria.

This lack of consensus between centres does not instil confidence in other health professionals who are asked to apply the criteria and offer appropriate surveillance to their patients. The publication of the Scottish guidelines aimed to address this lack of consensus. These guidelines are used in all four Scottish cancer genetic centres and applied to all cancer family histories assessed.

The assignment of a low risk to a family history will include some individuals that do have a family history of colorectal cancer but do not have a family history that meets moderate risk criteria as defined by these guidelines. This can be confusing for patients to understand especially if family members living outside Scotland are offered surveillance. Not all health professionals will feel confident to deal with this scenario and may refer to cancer genetic services inappropriately.

The results of this study have shown that 27 (1.8%) of 1509 cases giving their family history were assessed as high risk, 253 (16.8%) moderate risk and 1229 (81.4%) low risk, using Scottish guidelines. As the high-risk criteria of the Scottish guidelines are the modified Amsterdam criteria, two other studies which have published data from a colorectal cancer cohorts and assessed the number of cases with a family history that meet modified Amsterdam criteria are directly comparable. Andrieu et al (2003) found 6 (0.8%) families and Katballe et al (2001) reported 18 (1.5%) families meeting the criteria. Neither of these studies offered criteria that could be compared to the moderate risk family history of the Scottish guidelines to enable a comparison.

Family history eligible for referral to cancer genetic services

Following Scottish guidelines the 280 (18.6%) cases with a high or moderate family history should have been offered a referral to cancer genetic services. Of these 280 cases, 14 (5%) were correctly identified at increased risk and referred to cancer genetic services prior to recruitment to the study. Of the 14 cases referred with an increased family history, 8 (66.7%) were in the age group 16-54 years. It is relatively unusual for the GP to have a young patient diagnosed with a colorectal cancer and this may prompt

GPs to explore reasons for this and undercover information about genetic risk which can be associated with cancers at a younger age.

Published results from many cancer genetic studies encourage the referral of younger cases to cancer genetic services. However, the case diagnosed later in life may be the person that changes a family history from low to moderate risk or moderate to high risk highlighting the importance of enquiring about family history in all colorectal cancer cases.

Many of the family histories assessed in the study did not meet high or moderate risk status until after the diagnosis of the recruited case. There was a mean time interval of 21 weeks from diagnosis to study recruitment and during this period cases had contact with some or all of the following; GP, colorectal cancer surgeon, oncologist or CCNS. These professionals had the opportunity during the 21 weeks to identify a high or moderate risk family history.

When a patient presents to the GP with symptoms suspected to be due to colorectal cancer, it is most important to deal with the current symptoms. However there should be a mechanism for the family history to be addressed following any diagnosis because there are surveillance implications for both the cases and their first-degree relatives.

Although surveillance to prevent colorectal cancer is important for 'at risk' relatives, mutation analysis and microsatellite instability (MSI) testing can only be offered to affected individuals who should be offered the opportunity to discuss this further in a cancer genetic clinic.

Interestingly, for cases with a high or moderate family history risk (as assigned by Scottish guidelines) there was no association found with sex, site of cancer, and Dukes' stage at diagnosis, comorbidity or deprivation.

Conclusion

The results of this study show that 18.6% of cases have a family history that requires referral to cancer genetic services (according to Scottish guidelines) and that a very small percentage of these cases were actually referred to cancer genetic services.

Of the 280 cases with high or moderate family history, there was no association with any variable analysed with the exception of the age of referrals made to cancer genetic services. This suggests that families with a moderate or high family history risk are broadly similar to other colorectal cancers cohorts with no assigned family history risk.

These results highlight that more education is necessary to enable GPs and other health professionals to apply the guidelines to family history. This education should provide a basic understanding of assessing a family history and making an appropriate referral to cancer genetic services.

Perceived colorectal cancer family history risk

This study examined whether a diagnosis of colorectal cancer increased an individual's perception of their family history risk and how they dealt with that perceived increased risk. All cases were asked if they thought they had a family history of colorectal cancer. Of 1456 cases[25], 222 (15.2%) perceived that they did have a family history. In order not

25 53 cases of the 1509 were the only person in the family with colorectal cancer; as they were diagnosed under age 45 their family history is deemed at moderate risk. They would not have been expected to answer yes to perceiving a family history of colorectal cancer and were excluded from analysis.

to bias the replies, they were neither asked to specify their concept of a family history, nor to justify the reply. No guidelines were given on moderate or high risk of colorectal cancer and perceived levels of risk were not challenged.

Of the 222 cases declaring a perceived family history 23 (10.5%) had a high risk, 110 (49.5%) moderate risk and 89 (40.0%) low risk family history, as assessed using Scottish guidelines.

Having a perceived family history risk of colorectal cancer varied by deprivation group, in the most deprived group 68% of cases that perceived a family history did have a family history meeting high or moderate risk criteria opposed to 50% of the most affluent group. It may be that those in the most deprived group are more likely to know more accurate details on their extended family. The number of cancers in their family may therefore appear higher which may cause them to think more about their risk. The more affluent cases may have moved away from their family for career development and have less detailed knowledge of their extended family history or alternatively they may have a greater awareness that family history is a risk factor for colorectal cancer but not be aware of the risk criteria.

In contrast more affluent women with a family history of cancer appear to actively request that GPs refer to cancer genetic services (Holloway et al 2004). It has also been found that a higher proportion of women attending family history clinics with a perceived risk of breast cancer are in the more affluent group (Fraser et al 2003) and are more educated (Brain et al 2000).

From the 280 cases with a high or moderate family history there were 147 (52.5%) cases that did not perceive a level of family history risk when questioned. This result is not surprising as in a study of women it was found that 25% of them did not know that family history was a risk factor for breast cancer. This is similar to findings of a number of studies on perceived risk for breast cancer that found many women estimated their risk of breast cancer as low (Murabito et al 2001). In a study of women attending a breast cancer family history surveillance programme 27% of the women enrolled felt their risk of developing breast cancer was either none or very small (Kash et al 1992).

Two cases in the study answered that they did not perceive themselves to have a family history risk but the GP informed them that they should be referred to cancer genetic services.

Conclusion

These results suggest that the most affluent group are more aware that family history is a risk factor for colorectal cancer as previously identified for individuals with a breast cancer family history. They also suggest that the more deprived group know more about their family history but only when they have several members with cancer do they perceive a risk.

The results have shown that GPs do not routinely enquire about family history and previous research has shown that more affluent individuals request referral by their GP.

Referral to cancer genetic services

If a case responded yes to a perceived family history of colorectal cancer they were then asked if they had discussed this with their GP. Of the 222 cases that responded 'yes' to

having a family history, 76 (34.2%) cases had discussed their concern with their GP and 51 (22.9%) of these cases had a high or moderate risk status assigned by the Scottish guidelines. Of the 222 cases that perceived a family history risk, a total of 14 (6.7%) cases were referred to the cancer genetic services. In 2 of the 14 cases the family history was assessed as low risk using the Scottish guidelines. The other 12 (5.4%) cases were referred to cancer genetic services and were appropriately referred.

These findings from this study appear to indicate that GPs do not routinely ask about family history of cancer. This may be a result of their lack of confidence in assessing the risk as found by Fry et al (1999) or due to time constraints (Suchard et al 1999). Alternatively many GPs may not be aware of the existence of guidelines for family history of common cancer (Rose et al 2001). The results also suggest that they are not encouraged to investigate the best course of action when a patient raises a concern about family history.

It appears that a concern about family history risk is not sufficient for most individuals to raise the concern with their GP. A higher proportion of cases in the most affluent group (35.5%) compared to the most deprived group (30%) discussed concerns with their GP. The existence of this study is unlikely to have any bearing on the decision making of the GP to refer to cancer genetic services. GPs were only informed about the study after the case had been recruited. In contrast knowledge that the study would identify those with a family history requiring referral could be an explanation as to why there were few referrals from the surgical and oncology teams as they were fully aware of the study. The surgical team in each hospital identified eligible cases and informed

the study team. They knew that a family history would be taken and cases at increased risk sent information on their risk assessment.

It was not possible to collect information from non-participants with a family history of colorectal cancer on whether they were referred to cancer genetic services. Of the 14 (5%) cases of a potential 280 cases that were referred to cancer genetic services l2 (4.3%) had discussed their concern with their GP.

High-risk family history

A total of 27 cases had a high family history risk, 17 (62.9%) of these perceived an increased risk and discussed their concern with the GP but only three (11.1%) were referred to cancer genetic services. An individual with colorectal cancer and a high-risk family history should ideally be identified before surgery. This enables the surgeon to discuss with the case, more radical surgery to remove more of the colon, because of the increased risk of metachronous tumours (Van Dalen et al 2003). A high-risk family history should also alert the surgeon to the need for continuing endoscopic surveillance (as the Scottish guidelines,) rather than being discharged at 5 years post-operatively. Individuals at high risk should also be offered referral to the cancer genetic service, as they are eligible for mismatch repair gene analysis and advice on surveillance for other cancers such as endometrial, ovarian and stomach cancer (Vasen et al 1999).
When a case is identified with a high-risk family history, the first-degree relatives become 'at risk' relatives. The Scottish guidelines focus on the 'at risk' individual's requirements for surveillance however, to begin the process of identifying a gene mutation in a high-risk family, the focus shifts to the person with colorectal cancer. That person requires genetic counselling on mutation analysis, discussions on what the

outcome of mutation analysis could mean for them and their immediate family, and the options available to gene carriers, before consent can be taken for mutation analysis.

The obvious aim of a HNPCC surveillance programme is to prevent colorectal cancer in potentially many other family members. It is important that the individual with colorectal cancer is fully aware of the implications of a positive mutation analysis result, and the change in risk to their first-degree relatives if a gene mutation is found. That person also needs to be aware that if no mutation is found, the family remains at high risk and surveillance of the case and 'at risk' relatives should remain in place.

Moderate risk family history

In the study 253 cases were assigned a moderate risk family history of colorectal cancer and should be offered referral to cancer genetic services. Each case can be offered MSI testing of tumour material, It has been found that >90% cases with a known mismatch repair gene mutation also have microsatellite instability in their tumour (Jass et al 1998) and only 10-15% of sporadic colorectal cancer tumours demonstrate MSI (Ionov et al 1993). These finding have led to the development of triage testing by cancer genetic services. In Scotland, cases that are living, had colorectal cancer in the past and have a moderate risk family history are offered testing of their tumour material. Those cases shown to have microsatellite instability through MSI testing are then offered mismatch repair gene analysis.

Cases not wishing to be tested but who would be happy for testing to be available to family after their death can have DNA stored by the cancer genetic services. This may be discussed with the cases at time of family history assessment. All first-degree relatives

over age 35, of a case with a moderate risk family history, are eligible for enrolment into a cancer surveillance programme. The surveillance for those at moderate risk is less intensive than high-risk families. It is important that these individuals are made aware of their risk and that the cancer genetic services can offer a service to discuss their risk and the surveillance available to them.

In this study 253 cases had a moderate risk family history and in total 9 (3.5%) cases were referred to cancer genetic services. There is a great potential to improve this referral rate.

The results from this study have shown that the publication and dissemination of referral guidelines alone has not achieved appreciation in routine medical practice that family history is an important risk factor. This is not an unusual finding as this has been reported for many published guidelines even when adapted for local use. This would suggest that innovation is required to successfully implement these guidelines and audit is necessary to monitor the effectiveness of them.

It appears from the results of this study that there is a lack of knowledge in most health professionals and the general public regarding family history risk and availability of cancer genetic services. This lack of knowledge has resulted in those eligible for cancer genetic services not being identified.

Cancer genetic services could also foster closer links with the relevant teams in each hospital. A procedure could be developed to make referral to cancer genetic services simple but effective for surgery, oncology and cancer genetic services.

Surveillance recommendations for high and moderate risk individuals

The risk category assigned to a family history determines first whether surveillance is appropriate. For those with a high or moderate risk family history the risk category also determines the frequency of endoscopic surveillance offered both to cases and their 'at risk' family members.

Colonoscopy is the recommended surveillance in individuals with an increased family history of colorectal cancer (Vasen et al 1998, Jarvinen et al 2000). There are currently long waiting lists for colonoscopy for those with lower gastrointestinal symptoms in Scotland. Resources are not yet in place to meet the additional workload of a surveillance programme for the asymptomatic 'at-risk' population. Currently surveillance colonoscopies for individuals with a family history of colorectal cancer are carried out within the routine colonoscopy clinics.

In contrast, the population breast-surveillance and familial breast-surveillance programmes are operated separately from symptomatic breast clinics in the breast units. Therefore the pressure of surveillance asymptomatic women does not impact upon the breast units seeing symptomatic women. Furthermore the population breast-surveillance programme for women age 50-65 is funded separately from the symptomatic breast-surveillance services in Scotland.

The interval between colonoscopy and other cancer surveillance may differ throughout UK. Surveillance intervals recommended in Scotland for high risk individuals differ greatly from the surveillance intervals recommended for moderate risk individuals. This study found that 27 (1.8%) cases were assigned a high risk. Cases could be offered

testing and first degree 'at risk' relatives would also be eligible for two-yearly surveillance. Data from ISD has shown that 2726 individuals, age 16-79, in Scotland had a diagnosis of colorectal cancer in the year 2000 (ISD 2003). Assuming that the findings of this study can be generalised to all cases with colorectal cancer in Scotland, and applying the figure of 1.8% to individuals diagnosed in Scotland would result in 49 families having a high risk of colorectal cancer. These would require referral to cancer genetic services for mutation analysis; cases and first–degree relatives would also require two-yearly colonoscopy surveillance whilst awaiting the result of the mutation analysis. This surveillance would continue for all mutation carriers if direct gene testing was available to the family and for all first-degree relatives and cases where no mutation is identified in the family.

It has been reported that an average of four first-degree relatives will be 'at risk' per increased risk colorectal cancer family excluding parents (Rose et al 2001). Thus 196 'at risk' individuals will qualify for two-yearly colonoscopy using figures from this study. In addition, female cases and female 'at risk' individuals will require surveillance for ovarian and endometrial cancer, and some of these may opt for prophylactic surgery. In addition Scottish guidelines recommend upper endoscopic surveillance every two years after age 50 even if there is no gastric cancer in the family.

A further 253 (16.8%) cases in the study were at moderate risk when assessed using the Scottish guidelines. Assuming as above that this figure can be generalised to all cases in Scotland in the same age group and applying the figure of 16.8% to the number of individuals diagnosed in Scotland in the year 2000, 458 cases would be eligible for microsatellite instability testing (MSI). If each case has four first-degree relatives that

are eligible and interested in endoscopic surveillance 1832 asymptomatic individuals would require a surveillance colonoscopy in a year.

It is possible that the proportion with high and moderate family history is inaccurate due to under or over reporting of cancers in a family. Nevertheless, these are the best data available of this kind and could serve as a basis from which to estimate the cost associated with these recommendations. This in turn could inform any future economic assessment. There is evidence that surveillance of 'at risk' individuals from the high-risk group may prevent colorectal cancer (Jarvinen et al 2000). In contrast the surveillance recommendations in Scottish guidelines for the moderate risk group are not based on robust evidence and no cost-effectiveness analysis has been performed.

As cancer genetics is a relatively new discipline, many individuals are currently being screened by colonoscopy but have had no formal risk assessment made on their current family history. There is evidence that the number of colonoscopies carried out for family history concern would be reduced (Brampton et al 2002) if a formal family history assessment were made. In many parts of the UK surveillance for a moderate family history risk is offered 3-5 yearly. This was the situation in Scotland until the implementation of the Scottish guidelines, now surveillance for a moderate family history risk is offered at the age 35 (or current age before 55 years when attending the cancer genetic service) and if this colonoscopy is clear another is suggested at age 55 years. This a major change with the new guidelines being based on age and risk relative to the population (Dunlop 2002). It is unlikely that a randomised controlled trial will be carried out in this group of people, so it is important that data is recorded systematically

from individuals undergoing surveillance and from cases with moderate risk family history so that a future evaluation of these guidelines can be made.

There is evidence that screening individuals at high risk using colonoscopy can prevent them developing colorectal cancer. The cost of screening these individuals (at 2005 costs) every two years from age 30 until age 70 would be £4,600. The basic cost of colorectal cancer surgery, chemotherapy and 5 year basic follow-up costs is approximately £ 36,000 (www.dh.gov.uk). This does not include management of any complications of surgery or infection nor any other further surgery or treatment for metastasis.

There is little evidence on the merit of surveillance screening for the moderate group of individuals. However, the cost of colonoscopy screening, on two occasions, for moderate risk individuals in Scotland is approximately £600, significantly less than the cost of basic colorectal cancer surgery. Approximately 60 moderate risk individuals could be screened for one person developing colorectal cancer and requiring surgery. This is a very conservative estimate as the overall cost of caring for a person with colorectal cancer and the consequences of the disease is likely to be far greater than £36,000.

Implementing Scottish family history guidelines

When the Scottish guidelines for colorectal cancer family history were published, the target population was asymptomatic 'at risk' individuals with a family history of colorectal cancer and not individuals diagnosed with colorectal cancer. These guidelines pay inadequate attention to individuals with colorectal cancer and the impact that a diagnosis may have on their family history status. In addition to the lack of direction given in the guidelines for cases with colorectal cancer, they have not been updated to reflect the changes in cancer genetic services that can be offered to the case. Scottish

genetic centres now offer MSI testing on tumour material from living cases with colorectal cancer that have a moderate risk family history. The individual with colorectal cancer is seen within cancer genetic services to give consent to access tumour material and normal tissue stored within pathology departments at time of surgery. If this request is successful the specimens are sent to the laboratory for MSI testing. This service is clearly biased towards individuals that are aware of family history of colorectal cancer and are well enough to attend the cancer genetic services. Many cases with colorectal cancer will never be well enough or survive long enough to visit a cancer genetic service and a more systematic approach is required to capture these cases.

Many problems are currently experienced by cancer genetic services in Scotland regarding access to tumour material in pathology departments. Normally an individual 'at risk' attends cancer genetic services for a consultation on family history risk and is informed that MSI testing is available if an affected family member can give informed consent. If the MSI testing is found to be positive the normal practice is to obtain blood DNA for mutation analysis and in families with no living affected relative this cannot be offered. When MSI testing is negative, family history guidelines for family surveillance remains in place, whether high or moderate risk. Similarly, if an MSI positive result is found and mutation analysis does not identify a gene change, family surveillance remains in place.

The results of this study have shown the lack of use and interpretation of published guidelines for individuals with a family history of colorectal cancer. It appears that when an individual is diagnosed with colorectal cancer, this does not increase the likelihood that the guidelines are used.

When the Scottish guidelines were developed and published, the Scottish Executive funded five cancer genetic associates in Scotland to provide the genetic associate-led model suggested in the document. This was to provide a service for individuals with a family history of breast, ovarian and colorectal cancers throughout Scotland. As previously discussed, the cancer genetic services have had an increase in referrals predominantly for breast cancer. Wonderling et al (2001) reported from UK genetic departments that 61% of patients were referred because of concerns about breast cancer and only 16% and with a concern about colorectal cancer family history, and that there were almost twice as many referrals and consultations per million population in Scotland than in the rest if the UK. In Scotland the population risk for a woman to develop breast cancer is 1 in 11, and for both men and women to develop colorectal cancer it is 1 in 20. Using this data you would expect the referral rates for breast and colorectal cancer to approximately the same.

An improvement in the service for access to cancer genetic services for individuals with colorectal cancer and a high or moderate family history risk is required. The most important task for the improved service is the development of an education programme for GPs and other health professionals involved in the care of cases with colorectal cancer. This could involve the investment of a genetic counsellor on secondment to deliver the education programme. In a community trial of two models to manage breast cancer family history referrals (involving the author of this thesis) Campbell et al (2003) reported that during the two-year study period, there was enhanced communication between GPs and genetic nurses. Guidelines were issued to all GPs in South East Scotland who were involved in the study and presentations made to some GP practices. Referral rates to the regional clinical genetic department during this time increased by 48%, indicating the benefit of an education programme. Referral rates were greater in

the trial arm that deployed a clinical genetic nurse to work more closely with general practice.

GPs should not be the only professionals responsible for identifying a family history indicating increased cancer risk. This should be the responsibility of every professional that is involved in the care of individuals with cancer (Burton 2003). In the early stage of cancer diagnosis and treatment, an individual with cancer will have more contact with other health professionals than with their GP. All health professionals should have the skill to take a family history.

Public awareness of family history

The study has shown that all of the cases referred to cancer genetic services had raised the concern about family history themselves with the GP. This confirms the findings of Fraser et al (2003) and Campbell et al (2003). Of the 280 cases identified as having a high or moderate family history, 133 (47.5%) cases had a concern regarding their family history. However, only 51 (18.2%) actually discussed their family history concerns with the GP and 12 (4.3%) were referred to cancer genetic services. The remaining 147 (52.5%) cases with a high or moderate family history did not perceive they had any increased risk.

Recently there have been some bowel cancer awareness campaigns, with leaflets primarily focused on the awareness of symptoms. Only in recent years have the colorectal cancer charities published specific information on family history as a risk factor for colorectal cancer, the first patient information leaflet that detailed family

history risk for breast, colorectal and ovarian cancer was published by the Cancer Research Campaign in April 1998. This leaflet was specifically on cancer family history and would only be requested by individuals that are aware they had or perceive they had a family history. However, the charity advisors have noted that most individuals in contact with the colorectal cancer charities have had a diagnosis of colorectal cancer or are the relatives of the person with colorectal cancer and are coming with questions on cancer and cancer care rather than concerns on family history (personal communication). More recently, one charity has addressed this within a booklet on colorectal cancer with a section giving detailed information on family history risk (Cancer Bacup 2004). The aim of this booklet is that users will read the section on family history risk.

A mass media awareness campaign on family history of cancer may assist the general public in recognising a relevant family history. However there is a potential that anxiety would be raised by an awareness campaign. Recent research has shown that it would be possible to raise awareness for all and not increase anxiety in those with or without an increased family history (Leggatt et al 2000).

Such campaigns are a common method of disseminating health information to a large amount of people. However the NHS Health Development Agency recognises they have limited success and to maintain awareness levels requires continuing investment and continued short bursts of mass media activity.

As no awareness campaign on family history of cancer has been attempted within Scotland, it is not possible to comment on how successful this may be in meeting

objectives. However, it would be possible to develop material for a campaign in Scotland using current family history guidelines. The format should be comprehensible to the general public, without raising undue anxiety.

A family history awareness campaign would aim to improve the numbers recognising a relevant family history. An awareness campaign may also aim to increase the confidence of the public to discuss their concerns regarding family history of cancer with the GP. A family history information leaflet may help GPs to explain why a person can be or should not be referred to cancer genetic services. However, this is unlikely on its own bring about a significant change in referral practices and will need to be considered as part of a wider plan of action.

A recent information leaflet published in Scotland (*Appendix 7*) is an appropriate example of assisting the general public to understand what constitutes a relevant family history of colorectal cancer.

Although cases with an increased family history are only a small percentage of all cases with colorectal cancer, they give an opportunity to identify small numbers of early colorectal cancers or prevent a colorectal cancer developing. The identification of 'at risk' individuals and their entry into surveillance programmes may in the future make a small but significant impact by the early identification colorectal cancer or reduction in incidence.

Family history risk and lower gastrointestinal symptoms

In this study, family history assessment was conducted after recruitment and after recording data on symptom presentation so should not have biased symptom reporting.

The behaviour of the group that perceived they had a family history of cancer was analysed as it could be thought that perceiving a family history risk of colorectal cancer in relationship to lower gastrointestinal symptoms might change actions and thoughts when experiencing lower gastrointestinal symptoms.

There was no statistically significant difference between those perceiving and those not perceiving a family history risk, with respect to sex, discussing their symptoms with other people, inspecting the toilet or toilet paper before flushing.

Those perceiving a family history risk were significantly more likely to be in the younger age group, to think they had cancer before they were diagnosed, and to state that they had some knowledge of colorectal cancer symptoms. Surprisingly, they did not use this knowledge, or their suspicion they had cancer to visit the GP sooner than those not perceiving a family history risk. There was no difference in the median waiting time with symptoms of those perceiving a family history risk; this median waiting time was exactly the same as the waiting time of the whole cohort.

Conclusion

Of 222 cases perceiving a family history risk analysis of knowledge and behaviour variables related to lower gastrointestinal symptoms failed to identify any differences from cases not perceiving a family history. This would suggest that the worry of family history is not considered high priority as patients do not visit their GP more promptly

for advice nor do they make their concerns about family history more frequently known to their GP. Making the concern on family history known to a GP was found in this study to increase the likelihood that a referral to cancer genetic services would be made.

Despite the Scottish Executive developing guidelines to assist GPs in assessing family history risk, these appear to be under-utilised. It is possible that GPs and other health professionals have not yet realised there are NHS services available to individuals with a family history of colorectal cancer. A concentrated effort is required to increase GPs and other health professionals' knowledge of genetics in colorectal cancer, and to develop skills to record family history information. There is a need to develop health professionals' ability to assess and refer those at increased risk and reassure those who are not.

A public health campaign may increase the public's understanding of an appropriate family history of colorectal cancer resulting in more appropriate referrals to cancer genetic services. This study found that 52.5% of cases with a family history that met Scottish criteria for high or moderate risk were completely unaware of their family history risk. It is possible that information for the general public on colorectal cancer family history risk would increase the confidence to discuss their family history risk concerns with their GP.

Symptom Presentation

A secondary aim of this thesis was to describe lower gastrointestinal symptoms that were present at the first visit to GP.

This section of the discussion concentrates on the descriptive analysis presented in the results. Although a great number of published papers present similar data, there is no literature presenting these data for the Scottish colorectal cancer population. There are a few studies of colorectal cancer cases in specific areas of Scotland, but the current study represents 1540 cases diagnosed throughout Scotland. It is important to investigate whether the Scottish population differ from other colorectal cancer populations, given the high incidence in Scotland.

Admission to hospital

Information on admission to hospital was abstracted from hospital medical records, irrespective of whether or not a case had emergency surgery. In this study, 242 (20%) cases were admitted as emergencies. This is within the range found in other studies but may not be an accurate representation of the proportion admitted as an emergency in the Scottish population due to the recruitment bias noted.

These data have shown a statistically significant difference between tumour stage and mode of presentation with a greater percentage of Dukes' stage D tumours presenting as emergencies than electively. In this cohort, 16 cases (6.8%) of emergency admissions had a Dukes' stage D tumour compared to 29 (3.1%) in the elective group.

Cases not participating in the study were sicker than the participants; a higher proportion received palliative surgery because of more advanced cancer. Other studies have reported the trend towards the presentation of Dukes' stage D tumours as emergency rather than elective admission, but have not reported this to be statistically

significant. The statistically significant result in this study may be explained by the large sample size giving the power to detect more modest differences.

There was a trend in this study for the most deprived to be more likely to be admitted as an emergency. Similar findings have been reported by other published studies. It was also found that the median waiting time with symptoms was shorter in cases admitted as an emergency than in those admitted electively. This finding again confirms previously published results of other research groups in other study populations.
Symptom presentation is widely reported in the literature and the results from this study mirror other published studies, where it was possible to make comparisons. In this study each case was asked which symptom prompted them to visit their doctor. They were then asked if they had any of twelve symptoms were present before they reported to a GP.

A large proportion of this study cohort consistently reported only a few symptoms. These are rectal bleeding, change in bowel habit, and to a lesser extent marked loss of energy. At presentation to a GP, most cases had several symptoms, some of which were of longer standing than the symptom that prompted them to see their GP. The main symptoms reported at first visit to their GP were rectal bleeding, (in 492 (37.2%) cases) and change in bowel habit, (in 349 (26.4%) cases).

When considering all symptoms reported to be present at first visit to a GP, the most common symptoms were; change in bowel habit, (in 805 (53.6%)), rectal bleeding (in 768 (51.6%)), and marked loss of energy (in 603 (40.5%)). The same three symptoms were also found to be the highest percentages in colon and rectal cancer. Rectal cancer

cases were found to have rectal bleeding in 370 (73.7%) cases, change in bowel habit 307 (61.2%) and 152 (30.3%) marked loss of energy. Colon cancer cases were found to have rectal bleeding in 237(34.0%), change in bowel habit 317 (45.5%) cases and marked loss of energy 310 (44.5%).

Of the 333 cases that visited a GP with only one symptom, 162 (48.6%) cases had rectal bleeding, 67 (20.1%) cases marked loss of energy and 57 (17.1%) had change in bowel habit.

The finding that a high proportion of colorectal cancer cases presented with both rectal bleeding and a change in bowel habit is consistent across all published studies. Published NHS guidelines for referring a patient with suspected colorectal cancer concentrate on rectal bleeding and changed bowel habit as symptoms. These guidelines mainly focus on cases having no anal symptoms with rectal bleeding and a change in bowel habit to more frequent and looser consistency of stools. Within this cohort 1094 (81.2%) had no anal symptoms. Of the 768 cases with rectal bleeding, 512 (66.7%) had no anal symptoms. The 33.3% of cases with rectal bleeding that did experience anal symptoms had soreness, itching, could feel a lump, had discomfort in the anal region or were experiencing anal pain. Of 805 cases reporting a change in bowel habit, 743 cases gave information on change of frequency and in 473 (63.7%) cases had increased frequency. Only 430 cases answered the question about consistency and of these 416 (89.1%) cases reported that with the increased frequency they also had looser stools. The group below 55 years of age were more likely than the two older age groups to report rectal bleeding. In the cancer referral guidelines the age threshold for referral is 60 years in England and 50 years in Scotland. These results show that some younger cases would be missed using these guidelines.

Marked loss of energy is most likely to be present in those cases with a low haemoglobin level. This study demonstrated that those most likely to report marked loss of energy were female and in the younger age group. It may be that younger people feeling excessively tired are aware that it is abnormal and are likely to report to the GP, whereas older people may accept this as part of the ageing process.

Delay in presentation with lower gastrointestinal symptoms

The study aimed to investigate which factors affect the time individuals have lower gastrointestinal symptoms before presenting to a GP, with special attention given to deprivation and comorbidity. There is a wide literature on this topic but little on the effect of comorbidity and deprivation. The median waiting times for the whole cohort show that the longest waiting time with any symptom was 13 weeks for weight loss and marked loss of energy. The median waiting times for pain, nausea and vomiting were shortest, consistent with their impact on daily living. For the majority of symptoms the median waiting time before seeing a GP was 8-9 weeks, with the exception of rectal bleeding, where it was 6 weeks. The three symptoms, which show a statistically significant difference in waiting time from the median of the whole cohort is rectal bleeding, change in bowel habit and weight loss.

Cases with rectal cancer waited longer before presentation with a change in bowel habit and rectal bleeding than those cases with colon cancer. Where there was weight loss, colon cancer cases waited longer than those with rectal cancer.

These results give further evidence that rectal bleeding is the main presenting symptom and appears to be the 'decision-making' symptom that prompts a visit to a GP. The

results also indicate that change in bowel habit is not considered a priority symptom, as the waiting time is the same as most other symptoms included in the symptoms list. Change in bowel habit with change in frequency and consistency is one of the main symptoms for consideration in making an urgent referral. These data suggest that individuals are not aware that change in bowel habit is important once present for 6 weeks. This may be an area for a health campaign to focus upon.
Interestingly, of the symptoms which individuals in this study self-treated, change in bowel habit was the most common. The 137 (46%) cases self-treating had a change in bowel habit. This may have contributed to the relatively long waiting time before seeing a GP.

There was no association between median waiting time with symptoms and any Dukes' stage of tumour at diagnosis. However, for Dukes' stage D tumours the 75th centile of the median wait time with rectal bleeding, change in bowel habit, marked loss of energy, mucus in stools and tenesmus was much greater than the 75th centiles of any other Dukes' stage. In this group, it is possible that earlier presentation may have changed the Stage at diagnosis in some cases. Cumulative data on waiting time demonstrated that at 24 weeks 178 (27%) cases with change in bowel habit, 179 (23%) of cases with rectal bleeding and 192 (31%) with marked loss of energy had not reported their symptoms to a GP. Further analysis of waiting time and Dukes' stage at diagnosis support findings previously published that longer the waiting time with symptoms were associated with less advanced Duke's Stage at diagnosis (except for rectal bleeding which showed the opposite relationship).

The study found no evidence that age, sex, deprivation or comorbidity had any effect on the length of time an individual waits with symptoms before visiting a GP. Although no overall association was found in waiting time and gender. Symptomatic females were more likely to have visited their GP at four weeks with symptoms than males.

Presentation factors in colorectal cancer

Number of symptoms at presentation

The number of symptoms that were present at the first visit to the GP ranged from 1 through to 11 symptoms. The majority of the cohort had between 1 and 4 symptoms with a median of 3 symptoms at presentation. Further analysis of those cases with 1-3 symptoms and 4-11 symptoms showed that males reported more symptoms at presentation than females.

Development of new symptoms after referral to hospital

The referral guidelines for suspected colorectal cancer indicate that if an individual presents with symptoms meeting referral criteria they should be referred urgently, where as others should be referred for a non-urgent appointment. In Scotland there is no definition of urgent appointment, unlike the two-week wait in England. Those referred for non-urgent appointments can wait for several months to be seen at an outpatient department. In 581 (47.9%) referral letters in this study there was no indication of urgency. Therefore it is important that these individuals are encouraged to report any new symptoms that develop after their referral to hospital to their GP. They should understand that any new symptom that develops could indicate a greater risk.

This study showed that 490 (31.8%) of cases did develop new symptoms and the percentage reporting these to their GP varied. The symptoms that would have made a difference to risk for urgent referral are change in bowel habit, rectal bleeding and marked loss of energy. In this cohort, 48 (38.4%) cases developed change in bowel habit, 31 (33%) rectal bleeding 53 (57%) marked loss of energy but did not report these to their GP.

There was no difference in the sex distribution of those reporting new symptoms during the waiting time, but a statistically significant difference in age groups with a greater proportion of younger cases than older cases reporting each of these three symptoms. This may reflect a change in the attitude of younger people and how they use the GP service.

Age

The study found that younger cases were more likely to wait longer than 4 weeks with their symptoms, (77.3% of this younger group waited greater than four weeks opposed to 68.1% in the older age group). This could be due to the younger age group being more likely to think that piles were the cause of their rectal bleeding. Of those waiting more than 4 weeks 18.2% of the younger age group thought they had haemorrhoids compared to only 12.2% in the older age group. The younger age group were also more likely to discuss their symptoms with other people, (71.3% of the younger age group compared to 64.1% of the older age group discussed symptoms with another person). Other studies have found the most common reason given for not attending a GP with rectal bleeding was the certainty that the cause was haemorrhoids (Byles et al 1992, Crossland & Jones 1995).

When questioned on knowledge of cancer symptoms before diagnosis, the younger cases were also more likely to state that they had some knowledge of colorectal cancer symptoms than the older age group. This younger age group were also the most likely group to consider that they had cancer before their diagnosis (46.1% in the younger group thinking they had cancer compared to 35.6% in older group). This is surprising as the older age group would be more likely to have experienced friends or relatives with colorectal cancer than the younger group.

The younger age group were also more likely to inspect the toilet and the toilet paper before flushing. It may be that the older group was less honest in answering this question.

Younger individuals reporting rectal bleeding were less likely to have a rectal examination by the GP on the first visit (56.6% of the younger group with this symptom had a rectal examination compared to 69.8% of the older group). The GP may consider a diagnosis of cancer less likely in a younger person as rectal bleeding is relatively common in the younger population in the community (Thompson et al 2000).

Gender

Females were significantly less likely than males to have had a rectal examination by their GP when reporting rectal bleeding, (280 (69.1%) of males and 174 (60.8%) of females with this symptom had a rectal examination). Possible reasons for this have been published; lack of an available chaperone, lack of time or recent publicity of alleged sexual assaults on patients.

Females were more likely to report some knowledge of colorectal cancer symptoms before diagnosis, perhaps being more aware of health campaigns due to the high profile of breast cancer campaigns.

Males were more likely than females to inspect the toilet and the toilet paper. However, on finding rectal bleeding, they did not present any sooner to a GP than females.

Deprivation

Cases in the most deprived group were less likely to say that they had any knowledge of cancer symptoms before their diagnosis and less likely to inspect the toilet paper or down the toilet paper before flushing. These latter results are consistent with not knowing about symptoms of colorectal cancer and thus being less likely to look for bleeding in your stools. The study found a few other differences between the most affluent and most deprived groups but none of these differences were statistically significant. The most affluent group were referred after only one visit to GP more often than the most deprived group. This may be as a result of the most affluent group having more knowledge of colorectal cancer symptoms or being more likely to insist on earlier referral. The influence of private medical insurance may also be a factor. Although data on private medical insurance were not collected systematically, the research nurses commented that privately insured cases that visited their GP with symptoms that may be interpreted as colorectal cancer symptoms were referred immediately for investigations.

There was trend in this cohort (not statistically significant) for those in the most affluent group to be diagnosed at Dukes' stage A than those in the most deprived group. Younger cases were more likely than older cases to be diagnosed with advanced

tumours. This was not associated with waiting time with symptoms or deprivation group. The behaviour of tumours in the younger group may be more aggressive, raising the possibility of different tumour aetiology in younger cases.

The most affluent group were more likely to have rectal cancer and the most deprived group to have colon cancer, and this mirrors the data published for the Scottish colorectal cancer population by ISD in 2004.

Comorbidity

Comorbidity was not found to be associated with any of the variables studied with the exception of having a rectal examination. Cases with more comorbidity were more likely to have a rectal examination at first visit to GP than those with no comorbidity. 313 (52.0%) with comorbidity having a rectal examination compared to 196 (45.8%) cases with no comorbidity that had a rectal examination.

Conclusion

There were no differences in the presenting symptom or the symptoms present at first visit to GP, waiting time with symptoms and various other aspects of symptom behaviour prior to diagnosis of colorectal cancer with respect to age, gender, deprivation groups and comorbidity in cases.

Guidelines for referral of suspected colorectal cancer

At the development stage of this study, the referral guidelines available to all Scottish GPs were the SIGN guidelines for the management of colorectal cancer (1997). These differed significantly from the NHS (2000) guidelines for England and Wales. In April 2002, the Scottish Executive Health Department (SEHD) issued new referral guidelines

for suspected colorectal cancer. (SEHD 2002) The SEHD guidelines were very similar to the National Health Service (NHS) 2000 guidelines, but with the key additional recommendation to refer cases urgently if they met the high-risk criteria. NHS (2000) guidelines set a 'two-week standard' for high-risk cases being seen at outpatients. A secondary objective of this study was to provide information on cases meeting the Scottish referral guidelines and to collect data on the development and reporting of new symptoms. However, the lack of near complete case ascertainment, recruitment and missing data limited the ability of this study to report on this topic.

The data required to meet this aim were collected through a structured symptom interview and extracted from medical notes. Reported symptom data were available from 1540 cases and medical notes data from 1212 cases (due to problems accessing medical notes).

The problems with eligible cases not being offered the study information and thus only 41% of ascertained cases being successfully recruited to the study were not predicted. The study methodology that is most likely to achieve near complete case ascertainment in a large Scottish study is identification of cases through audit framework. This would require the systematic and prospective collection of data that is of acceptable quality for all colorectal cancer through out Scotland.

In 2002, the Association of Coloproctology of Great Britain and Ireland (ACPGBI.) published a reference paper with evidence to support the development of referral guidelines. Within this paper a range was given for the percentage of cases meeting specific referral criteria as reported in published studies.

A similar analysis by site of cancer by specific referral criteria was carried out in this study following the ACPGBI methods. Of the 1212 cases that had their medical notes accessed, 1199 cases had information on cancer site. Of these, 778 (64.9%) cases had rectal and sigmoid cancers and 421 (35.1%) cases had caecal or descending colon cancer.

The ACPGBI reference paper gave five referral criteria for rectal and sigmoid cancers and three criteria for caecal or descending colon. Of the eight criteria, five relied on access to medical notes for data on abdominal mass, rectal mass, haemoglobin levels and intestinal obstruction.

Rectal or sigmoid cancer

In those with rectal or sigmoid cancer there were three referral criteria that related to data on symptoms at presentation and two relied on data from the referral letter.

- 'Rectal bleeding with no anal symptoms' was found in 50-60% of cases assessed by the ACPGBI and 49.6% of this cohort.
- 'Rectal bleeding and change in bowel habit' was found in 50-60% of cases assessed by the ACPGBI and 39.2% of this cohort.
- 'Change in bowel habit to looser and/or increased frequency' was reported in >90% by the ACPGBI and was found in 50% of cases in this cohort.

There are reasons why such a wide discrepancy is seen:

- Cases in this study may have underreported their symptoms, due to recall bias.

- A high proportion of the advanced cancers in other studies displayed these symptoms and this group is under represented in this study.
- Hospital doctors have more experience in eliciting symptom information. The research nurses in this study simply asked the question and explained the meaning of some symptoms, if required.

'Rectal mass' was found in 40-60% on rectal examination and in this cohort it was found in 11.4% of the cohort.

'Left sided abdominal mass' was found in 20% of sigmoid cancers but there were no comparable data available in this study.

Cancers of the caecal and descending colon.

In those cases with caecal and descending colon cancers, three referral criteria were given that relied on data from medical notes.

The ACPGBI criteria predicted that a range of 30-75% of cases would have iron deficiency anaemia and 54% would have a haemoglobin level below 10g/dl.

In this study the data on haemoglobin level was available for 1212 cases. Haemoglobin level recorded the closest time to the referral letter or admission to hospital, if emergency admission was recorded. Adopting this approach reduced the bias that might be caused if an individual received a blood transfusion prior to surgery or soon after an emergency admission.

Iron deficiency anaemia was not defined in this section of the ACPGBI guidelines. This study analysed using a definition of Hb < 11 g/dl in men or < 10 g/dl in postmenopausal women, as given in the NHS 2000 guidelines. Of the cases in this study 27.9% had iron deficiency anaemia, and 84% of these had a level below 10g/dl.

'Abdominal mass' was given a range of 40-55% and this study found that abdominal mass was recorded for 9% of cases in this group. 'Emergency cases presenting with intestinal obstruction' was given as 10-30%, and 9% was found in this study cohort.

Results from this analysis confirm that the information on rectal and abdominal mass data taken from the referral letters cannot be assumed to be accurate. Much of the literature on which the ACPGBI paper was based was from hospital studies. There is a high probability that their data may represent the range of signs and symptoms elicited by specialists rather than GPs.

The uncertain quality of data from the GP referral letter limits the validity of the results. Detailed results on the proportion of this study cohort meeting at least one of the referral criteria (in the high-risk referral guidelines) are not presented in this thesis.

Conclusion and recommendations

The data collected for this section of the thesis were biased due to recruitment bias and uncertain validity of the data quality within the referral letters. The latter illustrates that an improvement in data capture from GP referral letters will be required if the assessment of referral guidelines is to be effective.

Using a standard proforma that incorporates the referral guidelines for patients with suspected colorectal cancer may have achieved better quality data. An example of a referral proforma for suspected colorectal cancer is included in (*Appendix 15*). This may have a role in reminding GPs of the referral guidelines and would assist in providing the accurate information required to assess the referral. This proforma may also reduce administrative time rather than producing an individual letter for each patient.

As GPs have previously stated that easy accessible, simple format guidelines would encourage implementation, this simple format may appeal to them. With current technology available to most GPs, it is feasible that this proforma could be completed on screen and emailed direct to surgical department. Alternatively, it could be completed on screen and printed out or hard copies could be available for manual completion. However this is implemented, previous research has shown that implementing any change of practice requires use of many different educational techniques, preferably on site and should include audit.

Data on urgency of the referral were collected from 1212 medical notes. Some referral letters also included the category of 'soon' and this was recorded as 'urgent' for data analysis. Of the 1212 medical notes accessed, 293 (24.1%) had no referral letter, 154 (12.7%) cases were referred as routine, 477 (39.4%) cases were referred as urgent and for 288 (23.8%) cases there was no indication given in the referral letter how the GP would like the referral to be treated.

The use of a proforma for referrals would improve the quality of data capture but would not address sample bias. To address sample bias in a study of this type, a Scottish audit would be required. This would also improve case ascertainment, the employment of a dedicated research nurses (as in the NTRAC initiative) may also facilitate high levels of

case of ascertainment as they would have access to cases at an earlier stage in their journey and would be known to the colorectal cancer team. However there will always remain a significant proportion of patients that will be genuinely too sick to be entered into a research project.

Implications for Health Service provision

Ascertainment and recruitment

This large population based study which recruited patients from 36 hospitals across Scotland and this experience of case ascertainment and recruitment may be valuable for other research studies wishing to recruit prospectively large numbers of cancer cases from Scottish hospitals.

Ascertainment was found to be higher in hospitals where a colorectal cancer nurse specialist (CCNS) was employed or where the recruiting research nurse was a previous member of staff. This suggests that employing a research nurse within each surgical cancer team or developing the research knowledge and role of existing staff members would facilitate ascertainment and recruitment of cases. Nurse specialists (in all areas of health care) can play an important role in epidemiological studies e.g. case/control studies and clinical trials that recruit cases in hospital. The CCNS has an explicit research function within their role and this research role should to be encouraged and developed in order to overcome the types of difficulties experienced with data collection in this study.

It would be advantageous to the NHS to provide further research training to develop a minimum level of research awareness and skills for all colorectal cancer nurse specialists, particularly as this specialist role demands involvement with local and National research

studies. This training would have cost implications for the NHS but could make a significant contribution to the success of Scottish cancer research initiatives.

Family history of colorectal cancer

Family history is now recognised as an important risk factor for colorectal cancer. Despite readily available published guidelines for GPs to assist with assigning a family history risk, this study has identified that the assessment of family history in patients with colorectal cancer is not routinely carried out by GPs.

This can have important consequences for the patient with colorectal cancer and their close family. If an individual with colorectal cancer is assigned a high risk family history risk they can be offered mismatch repair gene analysis and the identification of a mismatch repair gene mutation would allows other family members to be tested. Those family members without the gene mutation can be reassured and will not require surveillance and those that do have the gene mutation can be offered regular surveillance with the aim of preventing cancer developing in the future. For patients with colorectal cancer the identification of a high-risk family history can reduce the risk of developing a metachronous cancer through lifetime surveillance. Individuals with colorectal cancer assigned a moderate family history risk can be offered MSI testing and first-degree relatives over age 35 are eligible to enter into a colonoscopy surveillance programme.

To improve the service and reduce inequality of access to cancer genetic services for individuals with colorectal cancer with a high or moderate family history risk, all health professionals in secondary care involved with these individuals should be provided with education and training to develop their knowledge and skills. This staff training and

development should equip them with the skills to record family history information, make a basic assessment of risk and make an appropriate referral to the cancer genetic services.

The study found that only 14 (5%) of individuals from a potential 280 cases with high or moderate family history risk (according to published Scottish guidelines) were identified by their GP and were appropriately referred to cancer genetic services. Of these, 12 cases had perceived that they had a family history of colorectal cancer and discussed their concern with their GP and were then referred to cancer genetic services. Only two cases that did not perceive a family history risk were identified by the GP and referred to cancer genetic services.

These results indicate that the publication of guidelines alone is not sufficient to change practice, and investment is required to provide innovative methods encouraging the implementation of guidelines. In addition, acceptable methods to prompt GPs to investigate family history in patients with colorectal cancer should be developed. To reduce inequality in access to cancer genetic services it is suggested that, in addition to staff training and development, a change in the service provision is required.

Service development proposal

Two approaches are discussed below. The first approach aims to improve quality and equality of referrals to cancer genetic services and the second approach is to provide a more equal service to all colorectal cancer patients.

First approach–use of family history proforma

Following completion of an education programme a practice nurse, GP, hospital nurse or doctor at any outpatient appointment clinic or on admission to hospital could complete a family history proforma (an example of which can be seen in *Appendix 14).* This family history proforma would gather enough family history information to allow a decision to be made on the eligibility of the patient for referral to cancer genetic services, giving the patient the option to be referred.

This may require an increase in the number of cancer genetic counsellors in order to deal effectively with the possible increase of referrals. However, the reduction in inappropriate referrals may balance the increase of appropriate referrals.

Second approach– surgical department service

If the responsibility for identifying individuals with colorectal cancer and a high or moderate family history were devolved to the surgical unit, with the support of the genetic counsellors, more families would benefit from the cancer genetic services currently available. The use of a family history proforma *(Appendix 14)* could once again be used to assist with this task. This study has shown that a high proportion of cases not participating in this study were receiving palliative care and were unlikely to ever be well enough to attend an appointment at cancer genetic services. Families of the more sick patients would be denied access to cancer genetic services and thus inequality in service provision is created. Assessing patients within the surgical units is the approach that is the most likely to address this problem and reduce this inequality in access to cancer genetic services.

The introduction of this service would require colorectal cancer patients with a high or moderate family history risk to be identified preoperatively. This would enable staff to discuss the following options with individuals assessed with a **high-risk** family history:

- Discuss MSI testing at the preoperative evaluation; consent could be taken for MSI testing on tumour material.
- The Consultant surgeon will be informed of high-risk status and the need to discuss a possible change of surgical procedure.
- Referral to cancer genetic services at a suitable time, using the family history proforma, regardless of MSI test result.
- Give information in accordance with the guidelines that their first-degree relatives aged 30 and over should also be referred to cancer genetic services.
- Offer the opportunity to have blood taken for DNA storage only.

Colorectal cancer patients with a **moderate risk** family history could be offered:

- Discussion of MSI testing at the preoperative evaluation. Consent could be taken for MSI testing on tumour material. Those with MSI-positive tumours would then be informed of result and offered referral to cancer genetic services for genetic counselling on mismatch repair gene analysis.
- Information for their first-degree relatives who may be eligible for referral to cancer genetic services to discuss family history risk and surveillance, regardless of MSI status they should be seen in cancer genetic services.
- The opportunity to have blood taken for DNA storage only.

It is current practice in all Scottish genetic centres to inform the consultand of other relatives at risk. This information is offered verbally and in written form and no attempt is made to follow this up.

The main health service implication for implementing this service within the surgical units would be funding for staff training and for an increased number of laboratory tests.

Referrals to cancer genetic services in this study were predominantly of cases that had the confidence to raise their concerns about family history with their GP. This finding further suggests that the health service should invest in the training and staff development of relevant health care professionals in assessing family history and making management decisions in accordance with published guidelines.

Knowledge and awareness

The study found that individuals from the most deprived group reported that they had no knowledge of colorectal cancer symptoms more often than individuals from the most affluent group, suggesting that future health campaigns should target their literature and media campaigns to be inclusive of all socioeconomic groups.

Presentation with lower gastrointestinal symptoms

The study found that the most common symptom for which an individual will buy over the counter medication before visiting their GP is a change in bowel habit (to loose or more frequent stools). It is suggested that this may be due to the widespread media advertising of over the counter medication to promptly halt diarrhoea.

Although there is conflicting evidence on the association between waiting longer with symptoms and stage of disease, extensive waiting time with rectal bleeding and change in bowel habit will have an effect on overall health. This could impact on recovery and complications if individuals continue to use over the counter medications without visiting a GP. Although these medications do give advice in the small print, that a visit to a GP is recommended should symptoms persist, the health service should ensure that this message should have a more central focus on the packaging, particularly in older adults, if other symptoms are present or symptoms are not promptly relieved.

Referral guidelines for suspected colorectal cancer

The study found a lack of consistency in the information provided in the GP referral letter on the symptoms the patient was experiencing on visiting the GP or the GPs findings after examination of the patient's abdomen or rectum. This lack of information may affect decisions made by the unit receiving the referral letter. In addition, few referral letters gave details on the urgency of the referral. Any future evaluation on the value of the referral guidelines for 'suspected colorectal cancer' will require a functioning and complete Scottish audit system to be in place. This would ensure that the biases that were experienced in this study would be minimised. However for this to be successful action will also have to be taken to improve capture of the data provided by the clinicians referring patients for further investigation. This would best be achieved by the development of a referral proforma. This could incorporate the important features of the referral guidelines that would act to encourage best practice by GPs. An example of a referral proforma is included in *Appendix 15*. The proforma also has the potential to improve the hospital triage service so as to ensure prompt and appropriate treatment of patients.

Future research

Research skills of surgical nursing staff

Before implementation of any training programme to improve research knowledge and skills it is necessary to ensure that the training package is tailored to need. A mapping study is required to identify the current level of research knowledge and skills of all health professionals. This enhanced training and knowledge would provide skills that could be utilised to participate in clinical audit.

Family history of colorectal cancer

Following the development and implementation of a family history training programme, research should be undertaken to evaluate its effectiveness. This would assess the degree to which health professionals record family history accurately and make referrals to the cancer genetic services appropriately, according to the family history guidelines. Further research could also be undertaken to understand how information on risk is devolved through families and a quantitative study on the number of relatives from an affected individuals attend a genetic counselling appointment and the uptake of screening.

Research could be conducted by the four genetic centres in Scotland to assess the patient acceptability of referral to the cancer genetic services, at this stage of their cancer journey. This research would include collection of data on the number and quality of the referrals and source of referrals and would monitor the number of low risk referrals.

Future research should evaluate the acceptability of MSI testing at this stage of the colorectal cancer journey and should include an economic study to evaluate the economic impact of the introduction of MSI testing.

Presentation with lower gastrointestinal symptoms

The result from this study and from other published studies is that cancers with a more advanced Dukes' stage at diagnosis are associated with shorter median wait times for the majority of symptoms. This finding is counter-intuitive. This suggests that some tumours progress faster through the stages and are at a more advanced stage when symptoms are first obvious or even before symptoms present. It is also consistent with a proportion of patients with Dukes' stage D tumours having waited a particularly long time with their symptoms that might have been diagnosed with an earlier staged tumour if they had presented earlier. Further analysis of the study results showed that the waiting time at the 75th centile of Dukes' stage D tumours was significantly longer than any of the other Dukes' stages. Further investigation of this issue might reveal new knowledge about tumour aetiology and merits future investigation.

Alternatively, the reporting of symptoms was inaccurate in the group.

What this study adds to current literature

This thesis adds the following to the current literature:

- Health professionals do not routinely assess the family history risk of individuals diagnosed with colorectal cancer and an education programme would be necessary to provide the skills and knowledge necessary to carry out this task.

- Family history guidelines in Scotland require to be updated to reflect changes in clinical genetic services. They need to change to highlight to health professionals that these guidelines also apply to individuals with colorectal cancer with a high or moderate family history risk.
- Waiting times with lower gastrointestinal symptoms before presenting to a GP are not specifically associated with comorbidity or deprivation. The waiting time with symptoms, presentation of symptoms and Dukes' staging are similar to other published studies and provides data on the Scottish colorectal cancer population.
- The referral letter system practiced in Scotland could be improved by the use of a standard referral proforma that would assist in future audit of the referral guidelines.

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Appendices

Appendix 1

A randomised controlled trial of breast cancer genetics services in South East Scotland: psychological impact history

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Clinical

A randomised controlled trial of breast cancer genetics services in South East Scotland: psychological impact

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This study compared the psychological impact of two models of breast cancer genetics services in South East Scotland. One hundred and seventy general practices were randomised to refer patients to the existing standard regional service or the novel community-based service. Participants completed postal questionnaires at baseline ($n = 373$), 4 weeks ($n = 276$) and 6 months ($n = 263$) to assess perceived risk of breast cancer, subjective and objective understanding of genetics and screening issues, general psychological distress, cancer worry and health behaviours. For participants in both arms of the trial, there were improvements in subjective and objective understanding up to 4 weeks which were generally sustained up to 6 months. However, improvements in subjective understanding for the women at low risk of breast cancer (i.e. not at significantly increased risk) in the standard service arm did not reach statistical significance. Cancer worry was significantly reduced at 6 months for participants in both arms of the trial. The two models of cancer genetics services tested were generally comparable in terms of the participants' psychological outcomes. Therefore, decisions regarding the implementation of the novel community-based service should be based on the resources required and client satisfaction with the service.

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Keywords: breast cancer genetic risk counselling; service delivery; psychological impact

Media attention to scientific developments in cancer genetics has resulted in a greatly increased demand for cancer genetics services. These services aim to identify individuals who have inherited a significantly increased risk of cancer in order to counsel them about their risks and to offer appropriate risk management to reduce morbidity and mortality. There is a challenge to provide this information in ways that the lay public can utilise to inform their health-care choices without causing undue psychological distress. Individuals who are not at significantly increased risk also need appropriate reassurance without precluding an appropriate vigilance to symptoms of sporadic cancer. There is also a challenge to respond to these new developments within existing health-care budgets. Internationally, there is a lack of consensus about how best to deliver cancer genetic services (Steel *et al*, 1999) and an urgent need for empirical evidence to inform service development.

A survey of 22 regional cancer genetics services in the UK in 1998 reported that the predominant users of these services were women with a family history of breast cancer (Wonderling *et al*, 2001). Of the women who are diagnosed with breast cancer, about 10% report having a family history of the disease (Narod, 2002). Of these cases, only a small proportion will be due to inherited genetic mutations in one of the known susceptibility genes, BRCA1 and BRCA2. These genetic mutations give rise to increased lifetime risks of developing the disease, often at an earlier age than is the norm for sporadically occurring cases.

Brain *et al* (2000) showed that there was no difference in the effectiveness of multidisciplinary cancer genetics teams and breast surgeons in terms of psychological outcomes in the management of familial breast cancer in Wales. Secondary analysis of the data (Brain *et al*, 2002) showed some significant differences in psychological outcomes between groups of women at different levels of breast cancer risk. Only those women at low or moderate risk showed significant reductions in cancer worry and perceived risk of breast cancer. Satisfaction with genetic counselling was significantly lower in those women found to be at high risk of breast cancer.

In South East Scotland, a multidisciplinary clinic offering specialist cancer genetic risk counselling and screening to women with a family history of breast cancer has been held in the regional breast screening centre in Edinburgh since 1992. With growing waiting lists for the South East of Scotland familial breast cancer clinic, more stringent referral criteria were applied. GPs referring women judged to be at low risk were sent a letter explaining that no appointment could be offered when the criteria were not met. Referrals of women at relatively low risk were still accepted where the woman's presentation remained a particular cause of concern (e.g. high level of anxiety about breast cancer risk which was difficult for the GP to manage).

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An alternative model of cancer genetics services has been proposed (Campbell *et al*, 1995) whereby genetics nurse specialists could offer clinics within GP locality areas to carry out risk assessment, provide counselling for those whose risk was not significantly increased and mediate referral of those at higher risk to the specialist service. It was hoped this would provide improved support to primary care and better services for those at lower risk while encouraging more cost-effective use of specialist resources for those at increased risk of developing breast cancer.

We carried out a cluster randomised trial of this new model of service delivery comparing it to the existing multidisciplinary specialist service. This paper presents a comparison of the psychological outcomes of these two service models and across participant's level of breast cancer risk.

MATERIALS AND METHODS

Participants

Ethical approval for the study was obtained from the local ethics committee. An invitation to take part in the trial was sent to all general practices in Lothian ($n=125$), South West Fife ($n=54$) and Borders ($n=24$) Health Boards in South East Scotland. One hundred and seventy practices (84%) agreed to take part, 23 (11%) declined and 10 (5%) did not reply. This meant that 725 of the 828 (88%) GPs in practice across these three Health Boards agreed to refer patients into the trial. Practices were randomly assigned to either arm of the trial using a minimisation technique (Pocock, 1983, pp 84–86) to ensure that the two groups were balanced for size of practice, historical referral rate and social deprivation index.

During the period March 1998 to November 1999, any woman referred from participating GP practices to the regional clinical genetics department for breast cancer genetic risk counselling was invited to take part in the trial. To be eligible for the trial, women had to live in the region, be able to give informed consent and had to complete a baseline questionnaire. Women who were symptomatic or had been diagnosed with breast and/or ovarian cancer were excluded from the trial as were those who had previously consulted another clinic about their family history of cancer. Those who were ineligible to participate were offered the standard regional service.

Procedure

Potential participants were sent an information sheet and were invited to return the consent form to indicate whether they were willing to participate in the trial. Those who consented were then asked to complete a baseline questionnaire. Reminders were sent to all nonresponders after approximately 4 weeks. Only those who completed the baseline questionnaire were enrolled in the trial. Nonresponders and those who did not consent to participate in the trial were offered the standard regional service. The service offered to women who returned a completed baseline questionnaire was dependent on the arm of the trial to which their GP practice had been randomised.

Standard (regional) service Women were sent a family history form and a baseline questionnaire to complete. The family history form requested information about first-, second- and third-degree relatives. If the family history form was not returned, a letter was sent to the woman and to her GP to explain that no consultation was possible without this information. A genetics consultant (MS) and genetics nurse specialist (JC) assigned categorical risk assessments informed by published criteria (Table 1) using the information on the completed family history form. If necessary, further information and/or confirmation of relatives' diagnoses were obtained by a genealogist and from the Scottish Cancer Registry. When a woman was assessed as being at 'low risk' (i.e. not at significantly increased risk), she and her GP were sent a letter to explain this. Women assessed as being at 'moderate' or 'high risk', or where an adequate risk assessment could not be made from the information available, an appointment at the familial breast cancer clinic were offered. The clinic consultation offered more detailed discussion with a genetics consultant about risk status and with a specialist breast surgeon about options for risk management (i.e. breast cancer screening and, for 'high-risk' women, prophylactic mastectomy or chemoprevention). Clinical breast examination and mammography (where appropriate) were carried out at this visit. After this appointment, the patient's GP was sent a letter to summarise the issues discussed. All women were asked to complete a postal follow-up questionnaire 4 weeks and 6 months later.

Table 1 Criteria for assessing a significantly increased risk of breast cancer (Cancer Research Campaign, 1997)

A woman's risk of developing breast cancer is moderately increased if she has one of the following:

- A first-degree relative with breast cancer diagnosed under 40 years.
- Two first- or second-degree relatives on the same side of the family with breast cancer diagnosed under 60 years or with ovarian cancer.
- Three first- or second-degree relatives on the same side of the family with breast or ovarian cancer.
- A first-degree relative with breast cancer in both breasts.
- A first-degree *male* relative with breast cancer.

Novel (community-based) service All women in this arm of the trial were sent an initial appointment for one of the community-based clinics (held in a GP practice near to where they lived), run by a genetics nurse specialist (RC/RT). At the clinic, the genetics nurse specialist ascertained the woman's family history of cancer and compiled a family tree. This information was compared to published criteria (Table 1) to determine whether she was at significantly increased risk. When an adequate risk assessment could not be made during the appointment, further information and/or confirmation of relatives' diagnoses were obtained from the patient or medical records, before the patient was informed of their risk by letter. Women deemed not to be at significantly increased risk (i.e. in the 'low-risk' category) were offered information and reassurance and were discharged from the clinic. These patients and their GPs were sent a letter reaffirming their 'low-risk' status and summarising the issues discussed at the appointment. Women found to be at increased risk (i.e. in the 'moderate-risk' or 'high-risk' categories) were offered an appointment at the regional centre with a geneticist and genetics nurse specialist. All women were asked to complete a postal follow-up questionnaire 4 weeks and 6 months later.

Sociodemographic and objective breast cancer risk data

Women were asked to record their date of birth, marital status and educational level on the baseline questionnaire. Information about the category of breast cancer risk to which each woman had been assigned was derived from the clinical records.

Psychological measures

Subjective understanding Women were asked to rate on a 4-point scale from 1 (*not at all*) to 4 (*very much*) how well they understood each of four issues relevant to breast cancer genetic risk. The issues were:

1. How increased risk of breast cancer is passed on in families.
2. The significance of their own family history of cancer.

3. Whether there was anything they could do to reduce their risk of developing breast cancer.
4. What services were available to protect the health of people at increased risk of breast cancer.

Responses were summed to give a composite score for subjective understanding ranging from 4 to 16.

Objective understanding Participants were asked to consider a number of factual statements and to respond 'true', 'false' or 'don't know'. There were 10 statements about breast cancer genetics (e.g. 'Only a parent who has had breast cancer can pass on increased risk to their children') and 12 statements about issues surrounding mammography (e.g. 'Mammograms are used to detect early stages of breast cancer'). Statements were scored 1 (*correct*) or 0 (*incorrect/don't know*), and the number of correct responses combined to give total scores for *genetics understanding* (range 0–10) and *mammography understanding* (range 0–12).

Perceived risk of breast cancer Although a number of items were used to assess perceived risk of breast cancer, the results of one item were analysed for the purposes of this report. Participants were asked to indicate whether they considered their own level of risk to be *high*, *moderate* or *low*.

Psychological distress

(i) *General Health Questionnaire 30-item version (GHQ-30)* (Goldberg and Williams, 1988). This well-validated scale was scored using the GHQ method (0, 0, 1, 1) using a threshold of $\geqslant 6$ to screen for 'case-level' general psychological distress.

(ii) *Cancer Worry Scale* (Watson *et al*, 1998). This six-item scale (adapted from four single items, Lerman *et al*, 1991a, b) assesses concerns about developing cancer and their impact on daily functioning. Total scores range from 6 to 24 where a higher score indicates higher levels of worry. The psychometric properties of the scale have been shown to be satisfactory (Brain *et al*, 1999; Hopwood *et al*, 2001).

Health behaviours Several *ad-hoc* items indicated the extent to which genetic counselling may have influenced the women's health behaviour. Participants at 4 weeks were asked retrospectively about their health behaviours prior to counselling (i.e. the frequency of breast self-examination, smoking, drinking alcohol, trying to lose weight, eating bran and high-fibre foods, avoiding fatty foods, eating a balanced diet, taking exercise, looking after their health in general). They were asked to rate whether the frequency of any of these behaviours had changed since consulting genetics services (at 4 weeks) or in the last 6 months (at 6 months) on a scale from 1 (*much less than before*) to 5 (*much more than before*).

Statistical methods

Descriptive statistics were generated to describe the study participants. Differences between two independent groups were analysed with independent samples *t*-tests (two-tailed), Mann–Whitney, χ^2 (two-tailed) or Fisher's exact tests (two-tailed). A 2 (trial arm) $\times$ 2 (objective risk) repeated measures analysis of variance (ANOVA) was used to determine between-group differences and within-group changes over time (baseline, 4 weeks, 6 months) in psychological outcomes and possible interactions between trial arm, objective risk and time. Significant effects were followed up with *post-hoc* tests (independent samples *t*-tests, paired *t*-tests, ANOVA). χ^2 (two-tailed), Fisher's exact (two-tailed), Cochran's and McNemar tests were used to examine the impact of time, trial arm and objective risk on perceived risk and the proportion of participants suffering from 'case-level' distress. A significance level of 0.05 was used throughout. The data were analysed using SPSS for Windows version 10.00 (1999).

RESULTS

Participants

Figure 1 shows the progress of participants through each arm of the trial.

Baseline Over the study period, 574 women, referred for breast cancer genetic risk counselling, were invited to participate in the trial. Consent forms were returned by 451 women (response rate 79%), of whom 428 (75% of those invited) agreed to participate in the study. Three hundred and seventy-three of these women (87% of those who consented) returned a completed baseline questionnaire, 185 of whom were then assigned to the standard service arm and 188 to the novel service arm of the trial according to their GP practice.

4 weeks Of the 373 women who completed a baseline questionnaire, 276 also completed a 4 week follow-up questionnaire (74% of those who were enrolled in the trial), 147 from the

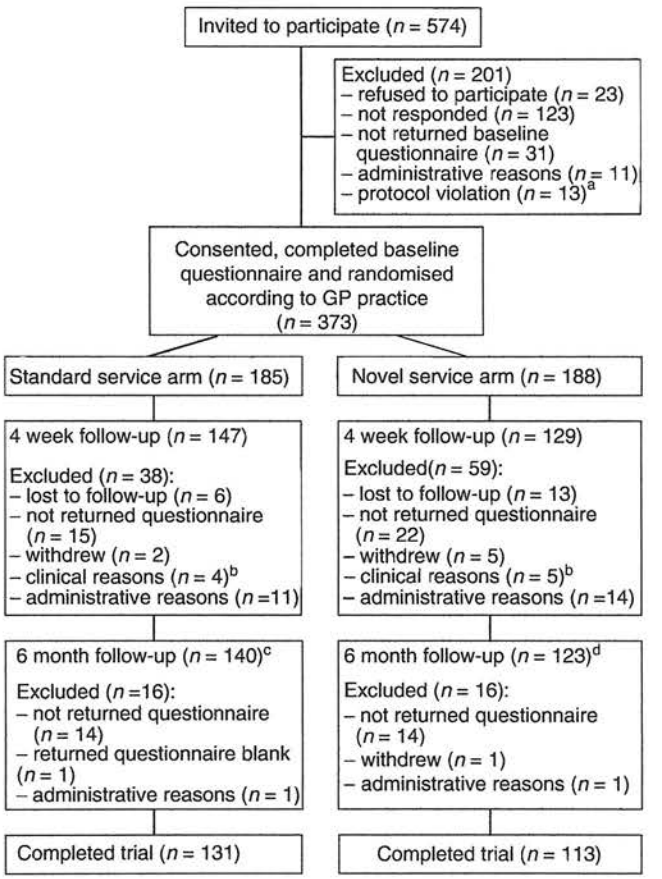

Figure 1 Progress of participants through the trial.
[a] For example, the women had received genetic counselling elsewhere or had been treated for cancer.
[b] For example investigation of breast symptoms.
[c] Includes nine women who were excluded at the 4 week assessment due to administrative reasons ($n = 5$) or nonreturn of the questionnaire ($n = 4$).
[d] Includes 10 women who were excluded at the 4 week assessment due to administrative reasons ($n = 4$) or nonreturn of the questionnaire ($n = 6$).

standard service arm and 129 from the novel service arm of the trial.

The characteristics of those for whom only baseline data were available ('baseline only group'; $n=97$) were compared with those of the '4 week group' ($n=276$) to check for participation bias. A significantly greater number of the 'baseline only group' had been assigned to the novel service arm than the standard service arm of the trial (61 *vs* 39%; $\chi^2=5.70$, df$=1$, $P=0.018$). A higher proportion of women in the 'baseline only group' were categorised as being at low risk (54 *vs* 32%; $\chi^2=14.01$, df$=1$, $P<0.000$). Similarly, a greater proportion of women in this group were suffering from 'case-level' distress at baseline (43 *vs* 31%; $\chi^2=4.53$, df$=1$, $P=0.043$). The 'baseline only group' had significantly higher scores at baseline on the Cancer Worry Scale (mean = 12.18/11.10; s.d. = 3.29/2.98; $t=2.97$, df$=367$, $P=0.003$). There were no significant differences between the two groups on any of the other sociodemographic or psychological variables at baseline.

6 months Two hundred and sixty-three women completed 6 month follow-up questionnaires (71% of those who were enrolled in the trial), 140 women from the standard service arm and 123 from the novel service arm of the trial. This includes 19 women who were excluded at the 4 week assessment due to administrative reasons ($n=9$) or nonreturn of the questionnaire ($n=10$). The baseline characteristics of those for whom the 6 month questionnaires were analysed ('6 month group'; $n=263$) were compared with those participants who completed the 4 week questionnaire but not the 6 month questionnaire ('Not 6 month group'; $n=32$) to check for participation bias. There were no significant differences between the number of women who dropped out from either arm of the trial. A greater proportion of women in the 'Not 6 month' group were classified as being at low risk of breast cancer (53 *vs* 31%; $\chi^2=6.41$, df$=1$, $P=0.016$). This group scored significantly lower on objective understanding of mammography ($t=-2.37$, df$=270$, $P=0.018$) and had a tendency to have higher scores on the Cancer Worry Scale ($t=1.83$, df$=290$, $P=0.068$). There were no significant differences between the two groups on any of the other sociodemographic or psychological variables (marital status and perceived risk could not be analysed due to small numbers in some categories).

Comparison of trial arms on sociodemographic and objective breast cancer risk characteristics

The sociodemographic characteristics of participants and the breast cancer risk category to which they were assigned are shown in Table 2. A greater proportion of women at low risk of breast cancer were in the novel service arm than the standard service arm of the trial at baseline ($\chi^2=11.86$, df$=1$, $P=0.001$), 4 weeks ($\chi^2=10.26$, df$=1$, $P=0.002$) and 6 months ($\chi^2=10.52$, df$=1$, $P=0.001$). Women with 4 week follow-up data in the novel service arm were somewhat older than those in the standard service arm ($t=-2.51$, df$=274$, $P=0.013$). There were no significant differences between the trial arms on any of the other sociodemographic variables at the three assessment points.

Table 2 Sociodemographic, objective breast cancer risk and psychological characteristics of the two trial groups at baseline, 4 weeks and 6 months[a]

	Baseline ($n=373$)		4 weeks ($n=276$)		6 months ($n=263$)	
Variable	**Standard service ($n=185$)**	**Novel service ($n=188$)**	**Standard service ($n=147$)**	**Novel service ($n=129$)**	**Standard service ($n=140$)**	**Novel service ($n=123$)**
Age (years): mean (s.d.)	37.3 (9.4)	39.1 (9.6)	36.8 (9.4)	39.7 (9.4)*	37.4 (9.5)	39.5 (9)
Marital status: *n* (%)						
Married/cohabiting	130 (71)	136 (73)	104 (72)	100 (79)	98 (71)	93 (77)
Separated/divorced/widowed	24 (13)	24 (13)	18 (13)	14 (11)	20 (14)	16 (13)
Never married	28 (15)	26 (14)	22 (15)	13 (10)	21 (15)	12 (10)
Education: *n* (%)						
To age 16 years	65 (36)	68 (37)	49 (34)	44 (34)	46 (33)	42 (34)
To age 18 years	30 (17)	28 (15)	23 (16)	19 (15)	23 (17)	15 (12)
After age 18 years	46 (26)	50 (27)	35 (24)	37 (29)	35 (25)	37 (30)
University graduate	39 (22)	40 (22)	36 (25)	28 (22)	34 (25)	28 (23)
Risk of breast cancer: *n* (%)						
Objective:						
Low	50 (28)[b]	81 (46)*	34 (23)	53 (41)*	31 (22)	50 (41)*
Moderate/high	129 (72)	97 (55)	113 (77)	76 (59)	109 (78)	73 (59)
Perceived:						
Low	5 (3)	7 (4)	12 (8)	10 (8)	11 (8)	11 (9)
Moderate/high	179 (97)	180 (96)	134 (92)	117 (92)	127 (92)	108 (91)
Understanding: mean (s.d.)						
Subjective[c]	9.4 (2.8)	8.9 (2.5)	12 (2.2)	11.7 (2.3)	11.9 (2.2)	11.7 (2.3)
Objective:						
genetics[d]	3.9 (2.5)	3.9 (2.2)	6.3 (2.3)	6 (2.2)	6.3 (2.2)	6 (2.1)
mammography[e]	7.3 (1.9)	7.0 (1.8)	8 (1.8)	7.8 (1.7)	7.9 (1.8)	7.9 (1.7)
GHQ-30:						
Total score: median (IQR)	2 (9)	2 (7.3)	1 (8)	2 (8.5)	0 (4)	0 (5)
'Case-level' distress: *n* (%)[f]	66 (36)	58 (31)	32 (21)	27 (22)	29 (21)	28 (23)
Cancer worry: mean (s.d.)	11.5 (3.2)	11.3 (3.0)	10.3 (2.4)	10.2 (2.7)	9.9 (2.5)	9.7 (2.7)

[a]Sample size varies due to missing data. [b]The majority of women who were assigned a low breast cancer risk in the standard service arm were informed by letter only. [c]Possible range of scores: 4–16. [d]Possible range of scores: 0–10. [e]Possible range of scores: 0–12. [f]Scores of $\geqslant 6$. *$P<0.05$.

Comparison of trial arms on psychological characteristics and changes over time (by trial arm and objective breast cancer risk)

Table 2 shows the psychological characteristics of the women in the two trial arms at baseline, 4 weeks and 6 months. There were no significant differences between the two trial arms on any of these variables at the three assessment points. Table 3 presents the results of repeated measures ANOVA for the 244 participants (65% of those who were enrolled in the trial) who completed the baseline, 4 week and 6 month questionnaires.

Subjective understanding Overall, there was a significant improvement in subjective understanding during the course of the study. Further analysis showed that subjective understanding only improved to a significant degree between baseline and 4 weeks ($t=-14.97$, df $=231$, $P<0.000$). Scores on subjective understanding were shown to be dependent on objective breast cancer risk. *Post-hoc* analysis revealed that women at moderate/high risk had significantly greater scores on subjective understanding than those at low risk at 4 weeks ($t=-2.69$, df $=235$, $P=0.008$) and 6 months ($t=-2.46$, df $=109.214$, $P=0.015$). The main effects of time and objective risk were modified by a significant interaction between these two factors. Subjective understanding had significantly improved for both women at moderate/high risk ($t=-13.70$, df $=164$, $P<0.000$) and women at low risk ($t=-6.55$, df $=66$, $P<0.000$) between baseline and 4 weeks. However, the improvement was significantly greater in women at moderate/high risk than those at low risk ($t=-2.51$, df $=230$, $P=0.013$). In addition, there was a significant interaction between trial arm, time and objective risk. *Post-hoc* analysis indicated that differences in subjective understanding between the risk groups within the different trial arms were significant only between baseline and 4 weeks ($F(1, 226)=5.27$, $P=0.023$). Between these two time points, the moderate/high-risk women in the standard service arm ($t=-11.64$, df $=98$, $P<0.000$) and low risk ($t=-7.32$, df $=41$, $P<0.000$) and moderate/high-risk women ($t=-7.58$, df $=65$, $P<0.000$) in the novel service arm had made significant improvements in subjective understanding. There were no significant differences in the extent to which subjective understanding had improved between these groups. Although for women at low risk in the standard service arm there was an improvement in subjective understanding between baseline and 4 weeks, this did not reach statistical significance.

Objective understanding There was a significant improvement in objective understanding of genetics and mammography across all participants during the study period. *Post-hoc* tests showed that scores on these two measures had significantly improved between baseline and 4 weeks only (genetics: $t=-14.37$, df $=232$, $P<0.000$; mammography: $t=-5.56$, df $=214$, $P<0.000$).

Cancer worry For all participants, there was a significant reduction in scores on the Cancer Worry Scale during the course of the study. *Post-hoc* analysis revealed that the greatest reduction in scores occurred between baseline and 4 weeks ($t=5.86$, df $=239$, $P<0.000$) with a smaller, but nevertheless significant reduction between 4 weeks and 6 months ($t=3.05$, df $=238$, $P=0.003$).

General psychological distress Although there was a significant decrease in the overall proportion of participants suffering from 'case-level' distress over the study period (Cochran's $Q=11.44$, df $=2$, $P=0.003$), further investigations showed that the reduction was only significant between baseline and 4 weeks (McNemar $\chi^2=8.27$, $P=0.004$). There were no significant differences in the proportion of women suffering from 'case-level' distress between trial arms or risk groups at the three assessment points.

Perceived risk of breast cancer There were significant changes in perceived risk of breast cancer across all subjects over the study period (Cochran's $Q=10.5$, df $=2$, $P=0.005$). Further analysis showed that these changes were only significant between baseline and 4 weeks where significantly less women perceived their risk as low at 4 weeks ($P=0.011$). There were no significant differences in perceived risk by trial arm at the three assessment points. However, a significantly greater proportion of women at low objective risk of breast cancer than those at moderate/high objective risk perceived their risk to be low at 4 weeks ($\chi^2=19.94$, df $=1$, $P<0.000$) and 6 months ($\chi^2=12.24$, df $=1$, $P=0.002$).

Comparison of trial arms on health behaviours

At 4 weeks, proportionately more women in the standard service arm reported examining their breasts every month as recommended (32 *vs* 23%) and proportionately more women in the novel service arm reported examining their breasts more frequently than once per month (11 *vs* 4%; $\chi^2=9.86$, df $=4$, $P=0.043$). There were no significant differences between the two trial arms in the extent to which participants reported performing health behaviours prior to genetic counselling or reported a change in these behaviours after counselling. At 6 months, there were no significant differences between the two groups in the proportion of women who reported changing any of their health behaviours in the last 6 months.

DISCUSSION

The present study responded to an urgent need for empirical evidence to inform the development of cancer genetics services in South East Scotland. A novel community-based service to provide genetic risk counselling for women with a family history of breast cancer was compared to the existing standard regional service.

The initial response rate to invitations to participate was good with 75% of the women invited agreeing to take part in the trial. The participation rates at each assessment point were satisfactory (baseline: 87%; 4 weeks: 74%; 6 months: 71%) with 65% of those enrolled in the trial completing all three questionnaires. The amount of data lost due to administrative reasons was comparable across the trial arms.

Women who dropped out of the study tended to be in the novel service arm of the trial or at low risk of breast cancer. The latter finding is not unexpected since these women may have been less motivated to continuing participating in a study of cancer genetics services which they were ineligible to receive. However, the women who dropped out of the study had greater levels of psychological distress. As these women may have dropped out in an effort to reduce their high levels of distress, they could perhaps benefit from further psychological intervention. Similar findings have been demonstrated by a previous trial of cancer genetics services (i.e. Brain *et al*, 2000). Given these potential participation biases, the results should be interpreted with caution in regard to their generalisability to a wider population.

The cluster randomisation strategy resulted in comparable trial arms at baseline in terms of sociodemographic and psychological characteristics. However, a greater proportion of women in the novel service arm were assigned a low risk of breast cancer. Further investigation is warranted to determine if this finding is due to chance or differences between the trial arms in terms of the method of risk assignment or the accuracy of family history details reported by participants.

At baseline, subjectively rated understanding of issues related to breast cancer genetic risk was relatively low (mean scores = 9.4 for the standard service arm /8.9 for the novel service arm out of a possible 16) and this was reflected in the objective assessment of understanding. On average, correct responses were given to about

Table 3 Repeated measures ANOVA for trial arm × time × objective breast cancer risk on psychological characteristics

Variable	Effect	F	df	P
Subjective understanding	Trial arm	0.244	1	0.622
	Time	107.82	1.675	0.000**
	Trial arm × time	2.092	1.675	0.133
	Risk	3.915	1	0.049*
	Trial arm × risk	0.032	1	0.859
	Time × risk	6.705	1.675	0.003*
	Trial arm × time × risk	3.234	1.675	0.049*
Objective understanding: Genetics	Trial arm	0.459	1	0.499
	Time	105.741	1.789	0.000**
	Trial arm × time	0.474	1.789	0.601
	Risk	3.31	1	0.07
	Trial arm × risk	0.708	1	0.401
	Time × risk	0.923	1.789	0.389
	Trial arm × time × risk	2.573	1.789	0.084
Objective understanding: Mammography	Trial arm	0.909	1	0.341
	Time	17.713	1.9	0.000**
	Trial arm × time	2.051	1.9	0.133
	Risk	0.857	1	0.356
	Trial arm × risk	0.068	1	0.794
	Time × risk	0.894	1.9	0.405
	Trial arm × time × risk	1.681	1.9	0.189
Cancer worry	Trial arm	0.117	1	0.733
	Time	36.9	1.62	0.000**
	Trial arm × time	0.535	1.62	0.549
	Risk	0.525	1	0.47
	Trial arm × risk	0.001	1	0.97
	Time × risk	0.127	1.62	0.838
	Trial arm × time × risk	2.675	1.62	0.082

*$P<0.05$. **$P<0.001$.

one-third of the breast cancer genetics items and to about two-thirds of the mammography items. About one-third of participants were suffering from 'case-level' distress. This is comparable to the findings in other samples of women prior to genetic risk counselling using the same measure and threshold (Cull *et al*, 1999, 2001) and to published data from the general population (Goldberg and Williams, 1988). Mean scores on the Cancer Worry Scale were similar to those reported in women prior to genetic risk counselling by Watson *et al* (1998) and Brain *et al* (2000) and slightly lower than those reported by Hopwood *et al* (2001) and Bish *et al* (2002).

The findings show that after consulting cancer genetics services, many of the short-term improvements in psychological outcomes experienced across participants were maintained up to 6 months. All participants reported greater subjective understanding of issues related to breast cancer risk and these improvements were most marked up to 4 weeks and were generally sustained up to 6 months. However, for the women at low risk of breast cancer in the standard service arm of the trial, unlike all other participant groups, these improvements did not reach statistical significance. This may be due to the fact that the majority of these women received a letter informing them about their low risk and were not offered a face-to-face consultation. Improvements in subjective understanding across participants were reflected by improvements in objective understanding which were again most evident between baseline and 4 weeks and were commonly maintained at a similar level up to 6 months. Although participants at low risk of breast cancer in the standard service arm did not feel that their subjective understanding had improved as much as the other participants, there were no differences between trial arms or risk groups in significant improvements on objectively assessed understanding.

It was reassuring to find that despite improvements in objective knowledge, the proportion of women suffering from 'case-level' distress decreased up to 4 weeks and cancer worry continued to decrease up to 6 months. Unlike previous research that found significant reductions in cancer worry only for those women at low or moderate risk of breast cancer (i.e. Brain *et al*, 2002), reductions in cancer worry in the present study were not dependent on objective risk.

Women's perceptions of their risk of breast cancer were altered during the course of the study with significantly fewer women overall perceiving their risk as low at 4 weeks, than at baseline. More women who were informed about a low risk of breast cancer perceived their risk of breast cancer as low following their risk assessment, as may be expected. Similar findings have been reported elsewhere (Bish *et al*, 2002). This suggests that the accuracy of perceived risk for the low-risk group improved during the course of the study. However, given the fact that responses to only one of the *ad-hoc* items were analysed for the purposes of this report and the accuracy of participants' risk perceptions was not assessed in this study, it is difficult to make any firm conclusions from these results. However, there is no evidence to suggest that learning that your risk of developing breast cancer is greater than you believed prior to genetic risk counselling causes psychological distress (Cull *et al*, 1999; Watson *et al*, 1999).

This study has shown that the novel community-based model of breast cancer genetics services is generally comparable to the existing standard regional service in terms of the psychological outcomes experienced by recipients. Therefore, decisions regarding the implementation of the novel model of services should be based on additional factors such as the resources required and

client satisfaction with the service. These factors have been investigated and will be published separately.

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Clinical

Appendix 2

Patient satisfaction with two different models of cancer genetic service in South East Scotland

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Clinical

Patient satisfaction with two different models of cancer genetic services in south-east Scotland

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There is a need to integrate primary- and secondary-care cancer genetic services, but the most appropriate model of service delivery remains unclear. This study reports patients' expectations of breast cancer genetic services and a comparison of their satisfaction with two service models. In the first model, risk assessment was carried out using mailed family history data. Women estimated as being at high/moderate risk were offered an appointment at the familial breast cancer clinic, and those at low risk were sent a letter of reassurance. In the second model, all women were seen by a genetic nurse specialist, who assessed risk, referred high/moderate-risk women to the above clinic and discharged those at low risk. Over 60% of all women in the study regarded access to breast screening by mammogram and regular check-ups as very important. This underlines the demand for a multidisciplinary service providing both clinical genetic and surgical services. Satisfaction was high with both models of service, although significantly lower among women not at increased cancer risk and thus not offered a clinical check-up and mammography. Increased cancer worry was associated with a greater expressed need for information and for reassurance through follow-up clinical checks and mammography. Better targeting of counselling to the expressed concerns and needs of these women is required to improve the service offered. GPs and patients expressed no clear preference for any specific service location or staffing configuration. The novel community service was less expensive in terms of both staff and patient costs. The potential to decrease health staff/patient contact time and to employ nurse practitioners with both clinical genetic and oncology training should be explored further. The rapidly rising demand for these services suggests that the evaluation of further new models needs to continue to be given priority to guide the development of cancer genetic services.

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Keywords: breast cancer; cost; expectations; genetic counselling; satisfaction

Media attention to scientific developments in cancer genetics and increased public awareness of the potential importance of a family history of cancer has resulted in a greatly increased demand for cancer genetic services. These services aim to identify individuals who have inherited a significantly increased risk of cancer in order to counsel them about their risks and to offer appropriate risk management to reduce morbidity and mortality. Genetic counselling for patients with a family history of cancer has been shown to result in a more accurate perception of risk (Evans *et al*, 1994) without an increase in anxiety (Hopwood *et al*, 1998). A survey of 22 regional cancer genetic services in the UK in 1998 reported that the predominant users of these services were women with a family history of breast cancer (Wonderling *et al*, 2001). Internationally, there is a lack of consensus about how best to deliver cancer genetic services (Steel *et al*, 1999), and an urgent need for empirical evidence to inform service development within the existing healthcare budgets.

A model of cancer genetic services has been proposed (Campbell *et al*, 1995, 2003; Fry *et al*, 2003), whereby genetic nurse specialists could offer clinics within GP locality areas to carry out risk assessment, provide counselling for those whose risk was not significantly increased and mediate referral of those at higher risk to the specialist service. It was hoped that this would provide improved support to primary care and better services for those not at increased risk, while encouraging more cost-effective use of specialist resources for those at increased risk of developing breast cancer. We have previously reported that the establishment of community-based clinics leads to substantially higher rates of annual referral, less evidence of inequity of access due to deprivation and improved referral practices (Campbell *et al*, 2003), but not to improved patient outcomes (Fry *et al*, 2003). In this study, we report women's expectations of cancer genetic services and the results of a trial assessing women's satisfaction with this new model of service.

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MATERIALS AND METHODS

Participants

Ethical approval for the study was obtained from the local ethics committee. An invitation to take part in the trial was sent to all general practices in Lothian ($n = 125$), south-west Fife ($n = 54$) and Borders ($n = 24$) Health Boards in south-east Scotland. In all, 179 practices (84%) agreed to take part, 23 (11%) declined and 10 (5%) did not reply. This meant that 725 of the 828 (88%) GPs in practice across these three Health Boards agreed to refer patients into the trial. Practices were randomly assigned to either arm of the trial using a minimisation technique (Pocock, 1983, pp 84–86) to ensure that the two groups were balanced for: size of practice; historical referral rate; and social deprivation index.

During the period March 1998 to November 1999, any woman referred from participating GP practices to the regional clinical genetics department for breast cancer genetic risk counselling was invited to take part in the trial. To be eligible for the trial, women had to live in the region, be able to give informed consent and to complete a baseline questionnaire. Women who were symptomatic or had been diagnosed with breast and/or ovarian cancer were excluded from the trial as were those who had previously consulted another clinic about their family history of cancer. Those who were ineligible to participate were offered the standard regional service.

Procedures

The service offered to women who returned a consent form and a completed baseline questionnaire was dependent on the arm of the trial to which their GP practice had been randomised. Details of the trial procedures have been described in detail (Campbell *et al*, 2003; Fry *et al*, 2003), but briefly the trial groups were:

Standard (regional) service Women were sent a family history form to complete. The family history form requested information about first-, second- and third-degree relatives. If the family history form was not returned, a letter was sent to the woman and to her GP to explain that no consultation was possible without this information. The genetic nurse specialist drew a pedigree from the information on the family history form, then assigned categorical risk assessments together with a genetics consultant using the criteria published by the Cancer Research Campaign (Cancer Research Campaign, 1997). If necessary, further information and/or confirmation of relatives' diagnoses were obtained from the cancer registry. When a woman was assessed as not being at a significantly increased risk (i.e. 'low' risk), she and her GP were sent a letter to explain this. An appointment at the familial breast cancer clinic was offered to women assessed as being at 'moderate' or 'high risk', and those for whom an adequate risk assessment could not be made from the information available. The clinic consultation offered more detailed discussion with a genetics consultant about risk status and with a specialist breast surgeon about options for risk management. Clinical breast examination and mammography (where appropriate) were carried out at this visit. After this appointment, the patient's GP was sent a letter to summarise the issues discussed. All women were asked to complete a postal follow-up questionnaire 4 weeks and 6 months later.

Novel (community-based) service All women in this arm of the trial were sent an initial appointment for one of the community-based clinics (held in a GP practice near to where they lived), run by a genetic nurse specialist. At the clinic, the genetic nurse specialist ascertained the woman's family history of cancer and compiled a family tree. This information was compared to the criteria published by the Cancer Research Campaign (Cancer Research Campaign, 1997) to determine whether she was at a significantly increased risk. When an adequate risk assessment could not be made during the appointment, further information and/or confirmation of relatives' diagnoses were obtained from the patient, medical records or the cancer registry before the patient was informed of their risk by letter. Women deemed not to be at a significantly increased risk (i.e. in the 'low-risk' category) were offered information and reassurance and were discharged from the clinic. These women and their GPs were sent a letter reaffirming their 'low-risk' status and summarising the issues discussed at the appointment. The women were asked to complete a postal questionnaire 4 weeks and 6 months later. Women found to be at increased risk (i.e. in the 'moderate-risk' or 'high-risk' categories) were offered an appointment at the regional centre with a consultant breast surgeon and a genetic nurse specialist. Prior to this consultation, they were sent a questionnaire asking for their opinions of the community clinic appointment and what further information or services they wished from the regional clinic. They were asked to complete a postal follow-up questionnaire 4 weeks and 6 months after their clinic appointments.

Sociodemographic and objective breast cancer risk data

Women were asked to record their date of birth, marital status and educational level on the baseline questionnaire. Information was also requested on mode of referral, knowledge of breast cancer and its inheritance, psychological status and details of what services and information was sought from the consultation. Information about the category of breast cancer risk to which each woman had been assigned was derived from the clinical records.

Data relating to the consultation

Clinic data The details of all clinic consultations were recorded. These included duration of consultation, level of risk stated, matters discussed, time spent in various clinic activities and outcome of the consultation. Matters discussed at the consultation were classified under five headings (family history and genetics; examination and screening; healthy lifestyles; other matters related to breast cancer and other matters unrelated to breast cancer).

Satisfaction with services received At the 4-week and 6-month follow-up, satisfaction with the consultations was measured in several ways. To assess general satisfaction, women were asked to assess a number of items from the Medical Interview Satisfaction Scale (MISS) (Wolf *et al*, 1978; used with permission from the author). We used 17 of the 26 original questions in the three subscales. The psychometric properties of this scale have been investigated in surveys in general practice with a conclusion that the MISS represents 'a valid and reliable instrument for the assessment of patient satisfaction with individual consultations in British general practice' (Meakin and Weinmann, 2002). Satisfaction with three aspects of a consultation were measured:

- *The affective aspect (A)*: The extent to which the respondent feels the medical professional (MP) listens, understands and is interested.
- *The behavioural aspect (B)*: The respondent's evaluation of the MP's competence in the consultation.
- *The cognitive aspect (C)*: Satisfaction with the amount and quality of information provided by the MP.

Each item on the scale was rated on a five-point scale of agreement from strongly agree (5) to strongly disagree (1). The summed scores were divided by the number of items answered by the subject to give mean scores for each aspect of the consultation and an overall mean score. An evaluation of the subscales within UK general practice has shown that they represent fairly discrete but overlapping aspects of satisfaction (Meakin and Weinmann, 2002).

We also investigated patients' assessment of the helpfulness of the specific information given and services offered at the consultation. We asked what additional information/services women would have wished to receive and what further action they had taken since their attendance at the clinic. We also asked about their preferences with respect to the clinic location and staffing.

Other measures Psychological distress and cancer worry were measured at baseline by the General Health Questionnaire (GHQ 30) (Goldberg and Williams, 1988) and the Cancer Worry Scale (Watson *et al*, 1998) as described by Fry *et al* (2003).

Relative cost of operating novel and standard service clinics
(a) *Estimate of staff costs*:
We estimated staff time taken for various aspects of the consultation (such as pedigree drawing, risk assessment and counselling) and travel time to clinics by asking the staff to complete a standard form recording these details. We also recorded details of women's attendance and nonattendance at clinics. Relative costs were based on a medical salary being two times that of a clinical genetic nurse specialist (consultant or associate specialist annual salary of £50 000 and clinical genetic nurse specialist salary of £25,000). The estimates also assumed that secretarial and administrative staff costs for the novel and standard service models were approximately equal, with the support for additional clinics in the novel service being offset by that for obtaining family history forms from all patients and the higher nonattendance rate in the standard service. A further assumption was that the efficiency of staff use within the clinics could be made approximately equal in the two service models by appropriate management of clinic sizes and appointments.
(b) *Estimate of patient time and financial costs:*
Patients were asked to complete a short questionnaire after clinic appointments asking them to give details of how they reached the clinic, their travel time and costs, details of any other costs (such as child care) and any loss of earnings and details of normal activities interrupted by the appointment.

RESULTS

Participants

Figure 1 shows the progress of participants through each arm of the trial with respect to the completion of questionnaires described in this report.

Baseline Over the study period, 374 women consented to take part in the trial and completed a baseline questionnaire. The age of the women ranged from 17.5–69.6 years with a mean ($\pm$s.d.) of 38.5$\pm$9.5 years. The characteristics of these women are described in a related publication (Fry *et al*, 2003). There were no differences in age, sociodemographic or educational factors between the two trial groups (Fry *et al*, 2003).

Follow-up The completion rates for the follow-up questionnaires are presented in Figure 1. A total of 274 (73%) completed 4-week and 265 (71%) women completed 6-month follow-up questionnaires. There were no significant differences between the questionnaire completion rates in the two arms of the trial.

Clinic consultations

Information was recorded on 379 clinic consultations. The genetics of breast cancer, the significance of the family history and the patient's own risk were discussed in almost all first consultations. In a large proportion (45–86%) of these consultations, there was also discussion of risks to children and other relatives and the possibility of finding a cancer predisposing gene. Mammography was discussed in almost all consultations. Screening for other cancers was much more likely to be discussed by the doctors seeing women who received the standard (regional) service. Breast self-examination and adoption of healthy lifestyles were more likely to be discussed by the nurse at the community clinic (novel service).

The length of time in minutes spent on each part of the consultation was not normally distributed in any of the consultation groups. The median total consultation time was 41 min for the community clinic appointment and 12 min for the regional follow-up appointment as part of the novel service; and 18 min for the regional appointment of the standard service. Women receiving the novel service spent more time at their initial community clinic appointment discussing each of the five areas of consultation (see above) than those receiving the standard service ($P<0.01$ to 0.001, Mann–Whitney test). Some of the increased time taken by the novel service was due to the fact that details of the family history had to be obtained at the community clinic appointment rather than by questionnaire as in the standard service.

Choice of clinic location and personnel At the 4-week follow-up, 107 (96%) women were satisfied with the length of community clinic appointment and 89–93% of women with that at the regional clinic. In all, 69 (30%) women did not state any strong preference for the location of a familial breast cancer clinic run by specially trained staff. There was a tendency for women to prefer the location of the clinic they had attended. The most popular choices were for a community clinic (selected by 27 (52%) of low-risk women who had received the novel service) and a regional clinic (selected by 51 (42%) women who received the standard service). Among the women who had attended both community and regional clinics, 23 (38%) preferred a community clinic and 16 (27%) a regional clinic. Overall, 115 (50%) of the women expressed no strong preference on the grade and type of staff and 58 (25%) preferred a genetic nurse and a consultant breast surgeon.

Expectations of the breast cancer family clinic

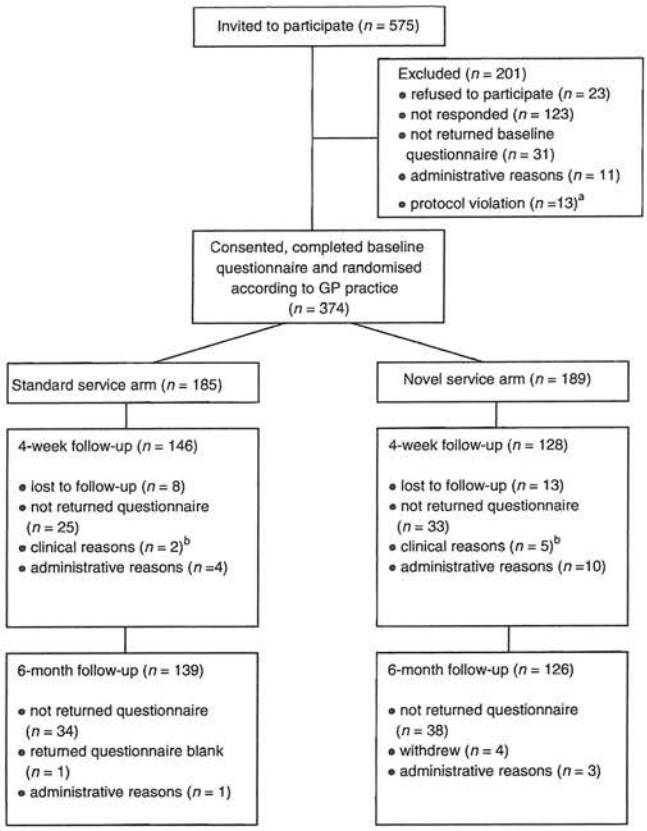
Information needs In all, 294 (79%) women said that they would like as much information as possible about their family history of cancer, but a minority of 35 (9%) wanted general information only and 43 (12%) only wished to know if their family was at increased risk. Women in the first group had significantly ($P<0.05$) higher cancer worry scores than women in the other two groups combined (Mann–Whitney test).

Women were asked to rate how important it was for them to get information about various specific issues. Items of information regarded by over 70% of women as very important are given in Table 1. Women less than 40 years attached greater importance to getting information about their risk than did older women ($P<0.01$).

Access to specific services Services for which access was regarded as very important by over 60% of women are given in Table 1. Women who placed great importance on the need for services to check their current cancer risk (those who rated the need for breast examination, check for current signs of cancer and mammography as very important) showed no difference in objective cancer risk or anxiety levels compared to those who did not. However, these women exhibited significantly greater cancer worry ($P<0.01$, Mann–Whitney test).

Assessment of services received

Patient satisfaction with services: overall satisfaction Table 2 summarises the median patient satisfaction scores by MISS



[a] For example, the women had received genetic counselling elsewhere or had been treated for cancer.

[b] for example, investigation of breast symptoms.

Figure 1 Progress of participants through the trial.

subscale and trial group. There were no significant differences by trial group.

Table 3 details the views of patients on specific aspects of satisfaction with services at the 4-week follow-up. The items are listed together with the aspect of the consultation measured and the number and percentage of patients who agreed/strongly (dis)agreed with the statement. A single satisfaction score was constructed as the mean of scores of all 17 questions. Most women were satisfied with the consultations in both models of service, with responses heavily skewed towards the 'satisfied' responses. When we considered factors that may have influenced satisfaction, no statistically significant correlation (Spearman rank correlation) was found between overall score and cancer worry (Cancer Worry score), anxiety (GHQ score), age or deprivation score. There was no significant difference between satisfaction in different educational groups (ANOVA). However, women assessed as 'low' risk were less satisfied with the services they received ($P<0.05$, t-test) than those assessed at 'moderate' or 'high' risk, as defined in this study.

Patient satisfaction with services: satisfaction subscales (see Table 3) The scores for the affective, behavioural and cognitive subscales in the MISS were not significantly correlated (Spearman rank correlation) with cancer worry (Cancer Worry score), anxiety (GHQ score) or age. There was no significant difference between educational groups in any of these scores (Kruskal–Wallis test). However, women at 'low' risk of breast cancer gave significantly lower mean scores for the affective (listening, understanding and interest of health staff) and cognitive (amount and quality of information given), but not the behavioural (competence of health staff) components of the satisfaction questionnaire ($P<0.05$, Mann–Whitney test).

Additional services requested by women A greater proportion of women who received the novel community service stated at the 4-week and 6-month follow-up that they would have liked additional services (Table 4). However, this is confounded by the higher proportion of women scored as low risk in the novel service trial group. Overall, in both trial groups 37% (24 of the 65) low-risk women wished access to other services. Low-risk women receiving the novel service noted mammography, breast examination, regular check-ups and screening for other cancers most commonly. Eight (19%) of these women at 4 weeks and seven (17%) women at 6 months wanted access to mammography. High- and moderate-risk women receiving the standard service most commonly noted screening for other cancers and genetic testing. At the 4-week follow-up, women who wanted further appointments to check their breast cancer status had higher cancer worry scores than other women ($P<0.05$, Mann–Whitney test).

Further action since attending clinic(s) Table 5 shows the number (%) of women (who completed both the 4-week and 6-month questionnaires) who stated that they intended to seek and had sought further advice about their family history of cancer after their clinic appointments. Overall, 42 (20%) stated that they intended to seek further advice and 18 (9%) actually sought further advice within 6 months. Most women simply wanted to keep up to date with new research or to find out about matters that they had not asked about at the clinic visits. A higher proportion of women receiving the standard service than the novel service (χ^2 test, $P<0.05$) and of women at moderate or high risk than low risk (χ^2 test, $P<0.05$) stated that they intended seeking such advice.

Women receiving standard service who did not attend a clinic but received a letter only

Women in the standard service group who were assessed at low risk were not offered a clinic appointment but were sent a letter explaining that they were not at increased risk of breast cancer. Some 22 (73%) of these women returned a questionnaire at 4-week and at 6-month follow-up. Although 15 (68%) found the information in the letter quite or very helpful, seven (32%) found it only a little helpful or not at all helpful.

Six (27%) and eight (36%) women, respectively, noted that there were other items about which they would have liked information at the 4-week and 6-month follow-up. Seven (33%) and eight (38%) women stated that they would have preferred a clinic appointment to a letter at the 4-week and 6-month follow-up, respectively.

Despite having been informed that their risk was not elevated, a large proportion of these women wished to have access to services and particularly breast examination (mentioned by eight (36%) at the 4-week follow-up and 15 (68%) at the 6-month follow-up) and mammography (mentioned by 14 (64%) at the 4-week and 15 (68%) at the 6-month follow-up). At the 4-week follow-up, only five women (23%) stated that they intended to seek further advice (for a variety of reasons) and by the 6-month follow-up, three (14%) had actually sought further advice.

Relative cost of operating novel and standard service clinics

Relative levels of staff costs in the two service models Based on the duration of appointments, the time taken by staff to carry out related duties, staff travel times, patient attendance rates and the assumptions detailed in the methods section, the novel service

staffing and travel costs were approximately 30% lower than those for the standard service.

Relative levels of patient costs in the two service models Questionnaires on time and costs associated with clinic attendance were completed by 164 patients attending the regional clinic and by 104 patients attending a community clinic. The median travel cost for attendance at the regional clinic was £1 (interquartile range, £1–£2.88) and for attendance at a community clinic was £1.00 (interquartile range, £1.00–£1.00). Travel costs were lower for women travelling to a community clinic ($P<0.001$, Mann–Whitney test). The travel time of women attending a community clinic was also less, with 15% of women taking over 30 min to reach the clinic compared to 50% of women attending the regional clinic ($P<0.001$, χ^2 test). In addition, only 2% of women attending a community clinic reported having to arrange care for their children compared to 12% of women attending the regional clinics.

Table 1 Information and service requirements of patients

Items of information regarded by over 50% of women as very important
The significance of their family history
Their own risk of breast cancer
Anything they can do in everyday life to reduce their cancer risk
How to examine their own breasts
Symptoms of breast cancer to look for
The pros and cons of breast screening
Research to find new or better ways to prevent/detect breast cancer
Breast cancer and its treatment
Services for which access was regarded as very important by over 60% of women
Reassurance that they show no signs of cancer now
Breast screening by mammogram
Regular check-ups

DISCUSSION

There is widespread recognition of the need to integrate primary- and secondary/tertiary-care services, but the most appropriate model of service delivery remains to be defined (Campbell *et al*,

Table 2 Median satisfaction subscale scores (with 25th and 75th percentiles) by trial group (modified MISS)

Patient group	Affective (A) scale	Behavioural (B) scale	Cognitive (C) scale
Novel service: all women	4.0 (3.6–4.3)	4.2 (3.9–4.6)	4.0 (4.0–4.6)
Standard service: all women	4.0 (3.7–4.4)	4.4 (4.0–4.6)	4.0 (4.0–4.8)

MISS = Medical Interview Satisfaction Scale.

Table 3 Numbers and percentages of women who agreed/strongly agreed[a] with various statements concerning their appointments

Statement	Aspect of consultation[b]	Novel service (community clinic) low-risk women	Novel service (community clinic) moderate/high-risk women	Novel service (regional clinic) moderate/high-risk women	Standard service (regional clinic) moderate/high-risk women
(a) I was told about my risk of developing cancer in words that I could understand	C	31 (91.2%)	77 (98.7%)	54 (96.4%)	82 (95.3%)
(b) After the consultation I have a good idea of what changes in my health I should seek medical advice about.	C	20 (64.6%)	67 (85.9%)	47 (85.5%)	65 (82.3%)
(c) At the consultation I was told all I wanted to know about my family history of breast cancer	C	26 (74.3%)	71 (93.5%)	47 (84.0%)	81 (92.0%)
d) The person I saw was very good at explaining the reasons for any medical tests which may be necessary	C	22 (81.4%)	67 (95.7%)	48 (88.9%)	76 (93.8%)
e) I feel I understand pretty well the plan for helping me	C	14 (56.0%)	67 (94.4%)	52 (96.3%)	79 (93.0%)
(f) I was given a chance to say what was really on my mind	A	30 (88.2%)	64 (90.1%)	46 (86.7%)	74 (85.0%)
(g) I really felt I was understood	A	22 (64.7%)	63 (87.5%)	43 (82.7%)	69 (84.2%)
(h) After the consultation I felt much better about my problems	A	16 (53.3%)	46 (69.7%)	39 (78.0%)	59 (76.6%)
(i) I felt the person I saw really knew how upset I was about my family history	A	19 (63.3%)	42 (75.0%)	35 (79.5%)	41 (64.0%)
(j) I felt free to talk about private thoughts	A	23 (71.9%)	46 (70.8%)	37 (77.1%)	48 (64.0%)
(k) I felt accepted as a person	A	32 (91.4%)	64 (91.4%)	50 (92.6%)	74 (93.7%)
(l) I felt that my problems were not taken seriously	A	24 (75.0%)	63 (92.7%)	43 (89.6%)	79 (96.3%)
(m) All the problems I mentioned were looked into	B	21 (70.0%)	57 (86.4%)	38 (90.5%)	60 (86.9%)
(n) I felt the person I saw did not spend enough time with me	B	32 (94.1%)	74 (94.9%)	54 (96.5%)	79 (94.0%)
(o) I was satisfied with the advice I was given about the courses of action I could take.	B	19 (59.4%)	75 (97.4%)	49 (90.8%)	75 (88.2%)
(p) The person I saw seemed rushed during the consultation	B	33 (97.0%)	75 (96.2%)	54 (96.4%)	80 (94.1%)
(q) The person I saw gave me too much information too quickly	B	30 (85.7%)	69 (88.5%)	49 (87.5%)	82 (94.3%)

[a]or disagreed/strongly disagreed items l, n, p, q. [b]A = affective aspect (doctor/nurse listens, understands and is interested); B = behavioural aspect (doctor/nurse competence); C = cognitive aspect (amount and quality of information provided by doctor/nurse).

1995, Donnai *et al*, 2000). This study reports on a cluster randomised trial of a novel model of service delivery and presents patients' expectations of cancer genetic services and a comparison of patients' satisfaction with two service models. Patient satisfaction is both an objective and outcome of care, and is therefore an important dimension of any consideration of the best configuration of patient services. In addition, satisfied patients are more likely to comply with advice given, which is an important aspect of any service in which patient information and advice comprises an important element of the intervention (Baker, 1991).

Expectations of cancer genetic services

About 80% of women stated that they wanted comprehensive information about the implications of their family history of cancer. The items about which women were most concerned to get information or receive services were those connected with their own risk and its possible reduction and early detection of breast cancer. Over 60% of women wanted a breast examination/mammography to have reassurance that they did not have breast cancer and regarded access to breast screening by mammogram and regular check-ups as very important. This underlines the demand for a multidisciplinary service providing both clinical genetic and surgical services, as noted by others (Brain *et al*, 2000). A recognition that increased cancer worry leads to a greater expressed need for information and for reassurance from follow-up checks is also important to guide clinical practice.

Assessment of cancer genetic clinics

Patient satisfaction with services received Levels of satisfaction with information given, staff attitudes and length of consultation were high. There were no significant differences between the trial groups. The lowest levels of satisfaction were found in those women with levels of cancer risk that were not significantly above population levels, and who were discharged with reassurance only. This reinforces the interpretation that many women seek a clinical examination to allay fears of current cancer (and possibly to have access to future screening such as mammography). It is also consistent with the previous finding that genetic counselling has less impact on general levels of patient satisfaction than other medical procedures, since it rarely 'suggests treatment or eliminates uncertainties' (Shiloh *et al*, 1990).

At the 4-week follow-up, 14% of the community clinic (novel service) group and 25% of the regional clinic (standard service) group stated that they intended to seek further advice, although the reasons for this were not primarily due to dissatisfaction with the service they received. The difference between the two low-risk and the two moderate/high-risk groups of women in the trial were not statistically significant. At the 6-month follow-up, only three women had actually attended another clinic for advice. Thus, provision of a community service staffed by nurses did not lead to an increase in the rate of care seeking after the consultation.

Clinic preferences GPs and patients expressed no clear preference for either model of service. Women who had attended a clinic consultation were approximately equally divided between expressing preference for a regional clinic, a community clinic and having no preference. One reason for this may be that many women are working and so may not find it any easier to get to a clinic near their home than to the regional clinic. Similarly, about half of the women had no strong preference when asked for their choice of clinic personnel. Among those who expressed a preference, the combination of being seen by a genetic nurse and consultant breast surgeon was the most popular.

Consultation times were greater when women were seen by a nurse at a community clinic (novel service). This is largely due to the time taken to document the woman's family history, but may also be because women feel more relaxed talking to a nurse or feel reluctant to take up the doctor's time. However, despite the shorter consultation times at the regional clinics, most women were highly satisfied with the duration of all consultations.

Management of women with a family history of breast cancer, but who do not have an increased risk

In all, 36% of women included in the study were not significantly above population levels of cancer risk. These women were less satisfied with the service received than women with a higher cancer risk. Most of these women were satisfied with the consultation. However, the novel service group was less satisfied than other groups of women with the amount and quality of information given. A relationship between patient satisfaction and rating of comprehension of the information received has been reported (Kincey *et al*, 1975), and failure to reassure has been linked to a failure to provide explanations at women's level of understanding. (Grande *et al*, 2002) It is possible, therefore, that the lower satisfaction reflects explanation and reassurance that is not targeted at the major concerns of these women which are a perceived need for examination for current (and future) cancer rather than principally a need for information about genetic risk. There is a need to tailor the explanation/reassurance by health staff

Table 4 Numbers (percentages) of women who stated that they would have liked additional services (not offered to them at the clinic consultation)

Patient group	4-week follow-up	6-month follow-up
Novel service: all women	26/115 (23%)	17/114 (15%)
Novel service; low-risk women	19/53 (36%)	11/50 (22%)
Novel service; high/moderate-risk women	7/62 (11%)	6/64 (9%)
Standard service: all women	23/124 (19%)	14/117 (12%)
Standard service; low-risk women	5/12 (42%)	1/8 (13%)
Standard service; high/moderate-risk women	18/112 (16%)	13/109 (12%)

Table 5 Numbers (percentages) of women who intended to and had sought further advice

Patient group	Intending to seek further advice	Had sought advice
Novel service: all women	14/ 99 (14%)	7/99 (7%)
Novel service; low-risk women ($n=42$)	5 (12%)	4 (10%)
Novel service; high/moderate-risk women ($n=57$)	9 (16%)	3 (5%)
Standard service: all women	28/111 (25%)	11/111 (10%)
Standard service; low-risk women ($n=8$)	0	0
Standard service; high/moderate-risk women ($n=103$)	28 (27%)	11 (11%)

to the background understanding and concerns of these women in order to improve services for these women.

More than a third of low-risk women who attended the community but not the regional clinic stated that they wished access to other services (most often mammography, breast examination, regular check-ups and screening for other cancers) at the 4-week follow-up, although this fell to 22% by the time of the 6-month follow-up. Thus, although most low-risk women were satisfied with being seen by a nurse at a community clinic, many still preferred to have the choice of accessing other services, even after being reassured that their risk is low.

Although most of the low-risk women, who received a letter of reassurance and advice but not a clinic appointment, found the letter quite or very helpful, about a third found it, at most, only a little helpful. A similar percentage said there were other items about which they would have liked information. In all, 50% stated that they wanted a check that they did not have current cancer, 64% that they wanted mammography and 77% that they wanted regular check-ups. At the four-week follow-up, 23% of this group said they intended to seek further advice and at the 6-month follow-up, 14% had actually done so.

Relative costs associated with the two service models

Since GPs (Campbell *et al*, 2003) and patients expressed no clear preference for any specific service location or staffing configuration, cost is likely to be a major determinant of the nature of these services in the near future. A preliminary comparison of staff time and travel costs in the two trial groups revealed that the novel (community) service was associated with approximately 30% lower staff costs with the assumptions given above. The staff costs of the novel service could be further reduced if the medium/high-risk women were referred to a specialist nurse for breast examination/mammography and did not have a second genetic counselling consultation (since new issues were rarely raised for discussion at this second appointment).

The costs of the standard service could be reduced if the moderate/high-risk patients were assessed at the regional clinic by nurse practitioners who were dually trained in genetics and oncology rather than by a medical consultant or associate specialist staff. This would reduce standard service staff costs to similar levels to the novel service.

It has been previously shown that being seen by nurses trained in breast care (including performing breast examinations for cancer) was acceptable to women and to GPs (Garvican *et al*, 1998). However, any new service model would first require to be evaluated with respect to patient outcomes and patient and staff satisfaction.

Costs to patients in terms of time and money were greater for attendance at the regional centre. This is consistent with the evaluations of other specialist outreach services (Bowling *et al*, 1997). However, since the low-risk patients, who were not offered an appointment at the regional centre, were the least satisfied it would appear that these costs were not a major factor influencing their preference for a particular service.

The potential to decrease nurse/patient contact time could be explored since shorter consultation times (at regional clinics) were not associated with lower levels of patient satisfaction or poorer clinical outcomes. Providing women with written and/or video information about the process and content of genetic counselling prior to their clinic attendance may be one way to achieve this and may in itself contribute to higher levels of patient satisfaction (Austoker and Ong 1994; Hallowell *et al*, 1997; Cull *et al*, 1998).

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Appendix 3

Referrals of women with a family history of breast cancer from Primary care to Cancer Genetic Services in South East Scotland

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Clinical

Referrals of women with a family history of breast cancer from primary care to cancer genetics services in South East Scotland

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As part of a cluster randomised trial to assess an alternative model of cancer genetics services, we gathered data on all referrals from general practitioners (GPs) to cancer genetics services in South East Scotland over a 4-year period. The referral rate per 1000 patients rose by 48% from 0.21 in the 2-year period before the trial to 0.31 during the trial. This increase was much greater in the trial group offered the GP clinic service (64% increase compared to a 38% increase in those referred to the regional service). Thus, the offer of a more local service appeared to have a marked effect on GP management of these women. Referral rates to cancer genetics services from general practices varied widely with higher referral rates from practices with more female partners. There was a negative correlation between referral rates and practice area deprivation scores. However, this was not found during the trial in the group which offered clinics in general practice, the provision of clinic appointments nearer to the homes of more socially deprived women resulting in improved access to women from deprived areas. The interaction with the GP appears to be associated with an inappropriate level of interest in and expectation of the appropriateness of genetic testing. The provision of the clinics within general practice did not result in higher levels of confidence among GPs in managing these women.
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Keywords: breast cancer genetic risk counselling; service delivery; primary care; deprivation

UK genetic services are based on a network of regional centres offering specialist services (diagnosis, risk assessment, counselling, surveillance and support) to families at high risk of serious genetic disorders. While links with secondary and tertiary specialists are established in most centres, links with primary care are in the process of development (Donnai and Elles, 2001).

Family history is known be a significant risk factor for breast cancer. Awareness of the genetic component of certain forms of cancer and therefore the potential importance of a family history is increasing among the population. This, in turn, has resulted in an increasing number of self-referrals to general practitioners (GPs), and subsequently to clinical genetics services (Campbell *et al*, 1995). A survey of 22 regional cancer genetics services in the UK in 1998 reported that the predominant users of these services were women with a family history of breast cancer (Wonderling *et al*, 2001).

Of women who are diagnosed with breast cancer, about 10% report of having a family history of the disease. We have recently found, in a large population-based survey of family history of breast cancer, that 52% of adult women have at least one first- or second-degree relative with breast cancer. Thus, all GPs will have many patients with first-degree relatives with breast cancer and many of these patients are likely to seek counselling and advice regarding their level of risk.

The aims and objectives of genetics services responding to the increasing public recognition of family history of cancer have been described in detail (Ponder, 1994). The provision of cancer genetics services has been seen as one of a number of cancer-control strategies located in primary care (Austoker, 1994). In South East Scotland, a multidisciplinary clinic offering specialist cancer genetic risk counselling and screening to women with a family history of breast cancer has been held in the regional breast-screening centre in Edinburgh since 1992. This clinic accepted direct referrals from GPs or other hospital consultants.

We had previously proposed an alternative model of cancer genetics services (Campbell *et al*, 1995), whereby genetics nurse specialists could offer risk estimation based on an assessment of the family history of cancer within clinics held in GP locality areas. This would be accompanied by appropriate counselling for those whose empiric risk was not significantly increased and by immediate referral to regional specialist services for those at higher risk. It was hoped that this would provide improved support to primary care and more appropriate services for those at lower risk while encouraging more cost-effective use of specialist resources for those at increased risk of developing breast cancer.

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We carried out a cluster randomised trial of this new model of service delivery comparing it to the existing multidisciplinary specialist service. As part of the data collection for this trial, we gathered structured data on all GP referrals to cancer genetics services in the South East of Scotland over a 4-year period. In this report, we present data on rates of referral of women to regional cancer genetics services for further assessment of their family history of breast or breast/ovarian cancer before and during the period of the trial. We identify and discuss factors that influence these referral rates and report the views of GPs about their role in the management of women with a family history of breast cancer and their attitudes to the services available to them.

METHODS

Referral by GPs to cancer genetics services

We defined a study population as the patients registered with general practices within the catchment region of the SE Scotland Cancer Genetics and Breast services. We calculated the total number of referrals from all 203 general practices in this region, which were approached to take part in the study during a 24-month period before the trial started and the 21-month period of the trial. The total number of patients on the lists of all these general practices was 1 221 261 at the beginning of the trial. The referral rate was estimated by

$$(\text{total referrals per year}) \times 1000 / (\text{total list size for all general practices}).$$

Thus, the referral rates to cancer genetics services before and during the trial were taken as the number of women referred per 1000 patients on the general practice lists during the periods from 1 May 1995 until 30 April 1997 and from 1 March 1998 until 30 November 1999, respectively. Referral rates for individual general practices were calculated in a similar fashion.

The Carstairs deprivation score that is based on postcode of residence was used as a measure of social deprivation of patients registered with general practices (Carstairs and Morris, 1990) with high positive deprivation scores being indicative of greater deprivation. For general practices in Lothian Region, deprivation scores for all patients registered with each practice were averaged to give a mean score for each practice. For general practices in Fife and Borders regions, individual scores were not available so we adopted the score for the postcode of the surgery address to represent the practice.

In order to assess whether differences in referral rates might be in part due to less selective referral criteria used by practices with higher referral rates (resulting in a greater proportion of women with a low risk of developing breast cancer), we classified general practices into four groups according to their referral rate during the trial. In each of these four groups, we calculated the proportion of referrals that were estimated to be at high, moderate and low risk based on an assessment of family history information given in the GP referral letter, thus reflecting the information available to the GP at the time of referral. In a few cases, the information in the GP letter was insufficient for an accurate risk assignment and so these women were omitted.

Women were asked if they had taken the first step by asking to be referred or if this had been suggested to them by their GP, a hospital doctor or another medical professional. Those who said that they had taken the initiative themselves were asked if this was because of their own concern, the suggestion of another family member, because of something in the press or for another reason.

Summary of the conduct of the trial

Ethical approval for the study was obtained from the local research ethics committee. An invitation to take part in the trial was sent to all general practices in Lothian ($n = 125$), South West Fife ($n = 54$) and Borders ($n = 24$) National Health Service (NHS) Boards in South East Scotland. A total of 170 practices (84%) agreed to take part, 23 (11%) declined and 10 (5%) did not reply. This meant that 725 of the 828 (88%) GPs in practice across these three NHS Board areas agreed to refer patients into the trial. Practices were randomly assigned to either arm of the trial using a minimisation technique (Pocock, 1983) to ensure that the two groups were balanced for size of practice, historical referral rate to cancer genetics services and social deprivation index.

During the period from March 1998 to November 1999, any woman referred from participating GP practices to the regional clinical genetics department for breast cancer genetic risk estimation and counselling was invited to take part in the trial. To be eligible for the trial, women had to live in the region, be able to give informed consent and to complete a baseline questionnaire. Women were asked to record their date of birth, marital status and educational level on the baseline questionnaire. Information about the category of risk to which each woman had been assigned was derived from the clinical records.

Women who were symptomatic or had been diagnosed with breast and/or ovarian cancer or who had previously consulted another clinic about their family history of cancer were excluded from the trial. Those who were ineligible to participate, nonresponders and those who did not consent to participate in the trial were offered an appointment by the regional genetics service. The service offered to women who were enrolled in the trial was dependent on the arm of the trial to which their GP practice had been randomised.

Women referred by the first ('regional clinic') group completed a family history form and those considered to be at increased genetic risk (i.e. in the 'moderate-risk' or 'high-risk' categories) received the existing service that comprised an appointment to see a consultant geneticist and breast surgeon at a regional centre. Women referred by the second ('community clinic') group were seen at one of several clinics held in a community setting relatively near the woman's own general practice.

At the community clinic, the genetics nurse specialist ascertained the woman's family history of cancer and compiled a family tree. This information was compared to published criteria to determine whether she was at increased risk. When an adequate risk assessment could not be made during the appointment, further information and/or confirmation of relatives' diagnoses were obtained from the woman or medical records or from cancer registry data, before the woman was informed of their risk by letter. Women whose risk of breast cancer was estimated not to be increased over that of women of a similar age in the general population (i.e. in the 'low-risk' category) were offered information and reassurance and were discharged from the clinic. These women and their GPs were sent a letter reaffirming their low-risk status and summarising the issues discussed at the appointment. Women whose risk was estimated to be increased over that of women of a similar age in the general population were offered an appointment at the regional centre with a consultant breast surgeon and genetics nurse specialist. Further details of the trial interventions are given in a related publication (Fry *et al*, 2003).

Psychological distress and cancer worry were measured by the general health questionnaire (GHQ 30) (Goldberg and Williams, 1988) and the Cancer Worry Scale (Watson *et al*, 1998) as described by Fry *et al* (2003).

Questionnaire survey of general practices who participated in the trial

All GPs who referred women during the study period received a questionnaire asking their views about various aspects of the management of women with a family history of breast cancer.

Statistical methods

χ^2 tests were used to compare the distribution of sources of referral before and during the trial, the risk statuses of women who were referred by practices with different referral rates, and the responses of women who had or had not been given information by their GPs. Comparisons were made between referral rates within trial groups using the paired *t*-test. Comparisons of the number of practice members and female practice members were made using the Spearman rank correlation coefficient since these were not normally distributed. Pearson's correlation coefficients were calculated between locality (Carstairs) deprivation scores and referral rates before and during the trial for all Lothian practices.

RESULTS

Referral rates to cancer genetics services

General practices approached to take part in the study A total of 203 practices in the Lothian, Borders and South-West Fife regions of Scotland were approached to take part in the study. Some 170 (84%) agreed to take part, 23 (11%) refused and 10 (5%) did not reply.

Changes in referral rates to cancer genetics services over time The referral rate (and 95% confidence interval) per 1000 patients on the GP lists rose from 0.21 (0.19–0.24) in the 2-year period before the trial to 0.31 (0.28–0.34) during the trial. Thus, there was a 48% increase in referral rate over this period of approximately 2.5 years, a highly significant difference ($P<0.001$).

Change in referral behaviour of GPs Prior to the study, many asymptomatic women with a positive family history were referred to the Edinburgh Breast Unit (symptomatic breast clinic) and then referred on, after receiving a mammogram and an appointment with a breast surgeon, to the cancer genetics clinic. In order to assess if there had been a change in this pattern of referral during the period of the study, we compared the referral sources of this group of asymptomatic women (with a positive family history of breast cancer) before and during the trial. The letter sent out at the start of the trial to all GPs requesting that referrals be directed to cancer genetics services rather than to symptomatic breast services was successful, with the proportion of referrals from the symptomatic breast service falling from 24.6% before the trial to 14.5% during the trial. There was a highly significant difference between the sources of referral before and during the trial ($P<0.001$).

Relationship between referral rate and risks of women referred Of the general practices that agreed to take part in the study, 30 referred no women during the study period. Annual referral rates during the trial for other practices varied by more than 30-fold, ranging from 0.05 to 1.66 per 1000 registered patients. The proportions of referrals that were estimated to be at high, moderate or low risk (based on information in the GP referral letter since this was the information available to the GP at that time) by four strata of general practice referral rates are given in Table 1. This shows that although general practices with the lowest referral rates referred a smaller percentage of low-risk women, there was no statistically significant trend in the proportions of risk classifications across the referral rate strata. Thus, we found no strong evidence that higher referral rates reflect the use of less selective referral criteria by these general practices.

Relationship between referral rates and number and sexes of partners in the practice Of the practices that had agreed to take part in the study, 15% had no female partners, 67% had one to two female partners and 19% had three or more. Neither referral rate before nor during the trial was correlated with the number of partners or the number of male partners in the practice. However, there is a small but significant correlation between both referral rates and the number (Spearman rank correlation coefficient 0.24, $P<0.002$; 0.23, $P<0.003$) and proportion (Spearman rank correlation coefficient 0.22, $P<0.005$; 0.17, $P<0.02$) of female partners in the practice before and during the trial, respectively.

Comparison between referral rates in the two trial groups Table 2 gives the mean referral rates before and during the trial-by-trial group. There was a statistically significant increase in referral rate between the two time periods in both trial groups (regional group $P<0.01$; community group $P<0.001$). This increase was greater in the community clinic trial group (64% increase compared to a 38% increase in the regional group over rates before the trial).

Relationship between referral rates and locality deprivation scores of general practices We calculated the correlation between the locality (Carstairs) deprivation score and referral rates before and during the trial for all Lothian practices (whether or not included in the trial) to investigate whether general practices serving women who were more socially deprived would have lower referral rates than those serving less socially deprived women. The correlation coefficients were −0.26 ($P<0.01$) with referral rates before the

Table 2 General practitioner (GP) referral rates (per 1000 patients on GP list per year) to cancer genetics services before and during the trial (mean and 95% confidence limits)

GP group	Before trial mean (95% CI)	During trial mean (95% CI)	Percentage increase in referral rate
Regional group	0.21 (0.17–0.26)	0.29 (0.23–0.34)	38.1
Community group	0.22 (0.17–0.26)	0.36 (0.29–0.43)	63.6

Table 1 Numbers (percentages) of referrals classified as high, moderate and low risk of breast cancer (due to family history based on national criteria) by practice groups with differing referral rates (annual rate per 1000 women on general practitioner list)

		Risk classification following national guidelines			
Referral rate during trial	Number of general practices	High risk	Moderate risk	Low risk	Total referrals
⩽0.19	41	7 (11.1%)	48 (76.2%)	8 (12.7%)	63
0.20–0.33	28	11 (13.3%)	55 (66.3%)	17 (20.5%)	83
0.34–0.54	39	26 (12.1%)	133 (62.1%)	55 (25.7%)	214
⩾0.55	31	23 (12.8%)	116 (64.8%)	40 (22.3%)	179
Total	139	67	352	120	539

trial and −0.13 (not statistically significant) with referral rates during the trial, suggesting that the tendency for practices serving less deprived areas to have higher referral rates was reduced during the time of the trial. Table 3 shows that the relationship between referral rate and locality deprivation score in general practices is influenced by the provision of community clinics. There was a negative correlation between referral rate and locality deprivation score both before and during the trial in the regional trial group. This indicates that practices in areas of lower social deprivation had higher referral rates. The same was true of the community trial group before the trial but during the trial the correlation was almost zero. Although the difference in referral rates between the two groups did not reach statistical significance, the lack of change in the regional but not the community trial group is striking (Table 3).

Patient's role in the referral by the GP In all, 43% of women indicated that they had asked to be referred (in contrast to the others for whom referral was suggested to them by their GP or another medical professional). Two-thirds of these women noted that this was based on their own concern with the others requesting referral at the suggestion of another family member. Younger women were more likely to have taken the initiative to request referral (50% of women under 40 years compared to 31% of those 40 years or over, $P=0.001$, χ^2 test).

Of those that stated that their GP (or other medical professional) had initiated the referral, only a third stated that they had specifically enquired about their family history of cancer; for over one-half the suggestion of referral had taken place when they had seen the doctor about another matter. There was no significant difference in educational status, perceived level of risk or cancer worry between the two referral groups.

Women's views of information given to them by their GP prior to referral

Women enrolled in the trial were asked questions about whether any information had been given to them by their GP about their family history of cancer prior to the referral. About 40% of women had received no such information. In total, 50% of those who had received information reported that they found it to be very helpful or helpful. Women were then classified into two groups according to whether or not they had received information.

The only statistically significant difference between the two trial groups (after correcting for the number of comparisons made (by the Bonferroni method) related to views on genetic testing. In all, 90% of those who had received information from their GP thought that it was very important or quite important to have genetic testing compared with 73% of those who had not received information from their GP ($P<0.01$). Similarly, 71% of the group who had received information from their GP stated any information from a genetic test would be very important compared with 56% of those who had not received information from their GP, but this difference was not statistically significant.

Table 3 Correlations between general practitioner-referral rates and locality (Carstairs) deprivation scores (higher score in more deprived areas) by trial group

Trial group	Correlation with referral rate before trial	Correlation with referral rate during trial
Regional group	−0.26	−0.28
Community group	−0.23	−0.01

General practitioners' views about the management of women presenting with a family history of breast cancer

All GPs who referred women during the period of the trial received a questionnaire asking their views about various aspects of the management of women with a family history of breast cancer. Completed questionnaires were received from a total of 129 GPs in the regional group and 115 GPs in the community group.

General practitioners' confidence in fulfilling their role in cancer genetics services Table 4 shows the percentages of GPs having various degrees of confidence in handling various aspects of the management of these women. General practitioners in both groups were most confident about taking a family history, providing emotional follow-up support and regular clinical examination and teaching breast self-examination. They were much less confident about calculating the risk and counselling on the basis of this and less confident about discussing the need for mammographic screening and deciding about whether a patient should be referred to the genetic clinic. There were no marked differences between the two trial groups suggesting that the limited number of contacts between the GPs and the genetics nurses who staffed the community clinics was insufficient to alter GP confidence in the management of these women. There was little evidence of GPs taking advantage of the presence of the nurse within the practice to discuss genetics issues.

General practitioners' attitudes to genetic counselling and active screening for family history of breast cancer Over 90% of GPs agreed or strongly agreed that cancer genetic counselling has a useful role for women with a family history of breast cancer, and over 85% agreed or strongly agreed that mammography has a useful role for those at increased risk. In contrast, however, only

Table 4 Percentages of general practitioners expressing their degree of confidence in fulfilling various roles in the management of women presenting with a family history of breast cancer

	Not confident or a little confident		Moderately confident		Confident or very confident	
	Regional	Community	Regional	Community	Regional	Community
Taking detailed family history	25.6	21.8	38.8	35.7	34.9	42.6
Calculating the risk	89.9	87.8	10.1	10.4	0	0.9
Counselling on risk	83.0	75.7	13.2	20.9	3.9	2.6
Providing emotional follow-up support	17.1	23.5	42.6	39.1	40.3	37.4
Providing regular clinical examination	29.4	21.8	37.2	40.9	33.4	37.4
Teaching breast self-examination	14.0	13.9	33.3	33.0	52.8	53.0
Discussing need for mammography/colonoscopy	28.7	33.0	42.6	41.7	28.7	25.2
Deciding whether patient should be referred to regional genetic clinic	41.1	45.3	50.4	38.3	8.5	15.7

Table 5 Percentages of general practitioners' stating views on the usefulness of various forms of support for the management of women with a family history of breast cancer

	Not useful or a little useful		Quite useful		Very useful	
	Regional	Community	Regional	Community	Regional	Community
Interactive computer program	34.1	37.4	47.3	36.5	17.1	22.6
Referral guidelines	9.3	6.1	45.0	43.5	45.7	48.7
Local clinics offering genetic counselling	27.2	20.9	44.2	42.6	28.7	33.9
Direct access to medical genetic screening	36.4	38.2	41.9	38.3	20.2	19.1
Training for yourself in genetic counselling	57.4	56.5	29.5	30.4	13.2	10.4
Training for other primary care staff in genetic counselling	64.3	56.6	27.9	30.4	7.0	11.3

30% agreed or strongly agreed that GPs should actively identify those from their lists who might be eligible for genetic counselling.

General practitioners' views on their information and training needs General practitioners' views on the potential utility of various forms of support from regional clinical genetics services in helping them deal with their increased workload are given in Table 5. Referral guidelines were considered to be the most useful support, with over 90% of GPs regarding them as useful or very useful. Local clinics offering genetic counselling were regarded by one-third as very useful. There was less enthusiasm for interactive computer programs or direct access to screening. Over 50% of GPs stated that training in genetic counselling for themselves or other practice staff would be not at all useful or only a little useful. It is possible, however, that this was due to their interpretation of the term 'genetic counselling' and that a higher proportion of GPs would favour some form of training to improve their skills. There were no differences in responses between GPs in the two trial groups.

General practitioners' views on trial interventions

About two-thirds of GPs (62% of regional group GPs and 65% of community group GPs) noted that they were confident or very confident about their women being seen by a genetic nurse specialist or genetic associate rather than by a consultant geneticist. A similar proportion (61% of regional group GPs and 64% of community group GPs) noted that they were positive or very positive about having genetic clinics in the community. When asked whether they would prefer community clinics run by nurse specialists or regional hospital-based genetic clinics about one-third (36% of regional group GPs and 34% of community group GPs) favoured the former and one-half (51% of regional group GPs and 50% of community group GPs) the latter, the remainder being undecided.

General practitioners found the structured summary letter the most useful aspect of the service followed by the provision of local community-based clinics (rated as useful or very useful by 44.4 and 37.4%, respectively). Other items (practice talks given by genetics nurse specialists and telephone advice) were rated as useful or very useful by less than a quarter of the GPs. General comments made by GPs included that they had made little use of the service and that women were less likely to default from appointments at community clinics.

DISCUSSION

Specialist outreach clinics

Specialist outreach clinics in general practice increased throughout the mid-1990s, reflecting a desire within the National Health Service to move towards closer integration of primary and secondary care services (Bailey *et al*, 1994). Within clinical genetics, it is recognised that this has the potential to lead to improved equity of access to high-quality regional services (Donnai and Elles, 2001), although this has not been formally evaluated. Within primary care, there has been a call to develop strong links with regional genetics centres. This has stressed the need to provide accurate information and support for the primary care team and to undertake some genetic risk assessment and counselling and facilitate appropriate referral within primary care (Kinmonth *et al*, 1998).

There have only been a limited number of thorough evaluations of outreach services across various disciplines. These have reported improved waiting times, patient satisfaction and convenience to patients but have noted less efficient use of specialist time, limited interaction between primary care and specialist staff and concerns about access to these services not being uniform throughout a region (Bowling *et al*, 1997).

Prevalence of family history of breast cancer and referral rates to cancer genetics services

We recently carried out a large cross-sectional survey of 13 155 patients registered with GPs in Scotland (Wallace E *et al*, personal communication). This found that a GP with an average caseload of 1700 patients would have 140 patients with a family history of breast, colorectal or breast/ovarian cancer, and of these 10 would meet national criteria for referral for risk assessment. Reported referrals to regional services for consultation regarding a family history of breast cancer suggested a referral rate of about 0.25 referrals per 1000 patients per year, consistent with the referral rates found in this study. This is based on referral of patients who presented spontaneously to their GP and not on any form of active surveillance by GPs of family history of cancer within their practice population.

During the study, there was nearly a 50% increase in referral rate, compared with 1–3 years prior to the study and a greater proportion of referrals came directly from GPs. At the start of the study period, local protocols, based on UK recommended guidelines for the primary care management of people with a family history of breast cancer, were developed together with GP representatives and Health Board guidelines groups. These local protocols were disseminated to all GPs in South East Scotland. In addition, all GPs received a biannual genetics update newsletter during the course of the study. These factors are likely to have contributed to the increase in referral rate.

A striking finding was the substantially greater increase in referral rates from pretrial levels in the community clinic trial group compared to the regional group (64% increase compared to a 38% increase). Thus, in addition to the underlying general increase in referral rates, the establishment of community clinics resulted in a change in referral behaviour that resulted in a further increase in referral.

Despite the increase in referral rates that we recorded over this 3-year period, these rates are considerably lower than those (15 out of 1000 adult women/year) at which women reportedly raise concerns about family history of breast cancer with their GP (Kinmonth, 2001) suggesting that the GP 'gatekeeper' role is an important one.

There was a very wide (more than 30-fold) variation in the annual referral rates. The reasons for this are not clear, but there was a small but significant correlation between referral rates during the trial and the number and proportion of female partners in the practice. Referral rates were greater from those practices with a greater number of female partners and this could be because women with a family history are more likely to seek the advice of a GP, if the GP is female. Thus, if the patient belongs to a practice where it is impossible or more difficult to see a woman, they may be less likely to seek advice. Alternatively, it could be that female GPs are more likely to refer women for genetic counselling about breast cancer risk than male GPs.

We postulated that higher referral rates may reflect the use of less rigorous selection criteria by some GPs. For example, this might have occurred because of their knowledge that selection, according to risk, for referral to the breast-screening service would be performed subsequently by the genetic nurse who interviewed the woman at the locality clinic. However, we found no evidence that this had occurred.

We interpret our finding as follows. Family history of breast cancer is common and many women consulting their GP may mention this at the time of consultation (Kinmonth, 2001). We found that younger women are more likely than older women to raise this concern and request referral to specialist services. General practitioners are operating at different thresholds at which they take action on these concerns. We have already shown that about 10% of women with a family history of breast cancer had been referred to a specialist service by their GP (Wallace E *et al*, personal communication). Once the decision to respond to this concern is made by the GP, similar referral criteria are applied. Currently, a more active surveillance of family history of cancer in primary care (which would result in a much higher referral rate) is not recommended in national cancer genetics guidelines nor is it supported by GPs (in this survey only 30% agreed that GPs should actively identify those from their lists who might be eligible for genetic counselling).

Relationship between deprivation and referral rates to cancer genetics services

There is an extensive literature that confirms that people from different socioeconomic groupings consume health care in different ways. This almost invariably shows that more deprived people have worse health and have greater need for health care (Balarajan *et al*, 1992; Eachus *et al*, 1996). It has been found that 15–20% of the overall variation seen in the overall GP referral rates (to all services) can be explained by deprivation (Hippisley-Cox *et al*, 1997). Disadvantaged groups have also been shown to be less likely to attend for breast and cervical screening preventive services (Eachus *et al*, 1996).

Provision of health care should be primarily determined by need. However, access to secondary care has been reported to be selectively poorer in deprived groups (Chaturvedi and Ben-Shlomo, 1995). In this study, the correlation coefficient between deprivation score and referral rate remained unchanged in the regional group: −0.26 before the trial and −0.28 during the trial. Thus, prior to and during the study in the regional group, there was a tendency for practices serving less deprived areas to have higher referral rates. The differential use of cancer genetics services across deprivation groups may be influenced by factors such as perceived risk and financial considerations (Eachus *et al*, 1996) or by health behavioural factors involving knowledge of importance of family history, how personal risk is perceived and what action is taken to seek counselling for a personal assessment of high risk and the ability to articulate need to health service staff.

However, this relationship changed in the community group with the establishment of new community clinics with the correlation between deprivation score and referral rate before the trial (−0.23) falling to −0.01 during the trial. Thus, the tendency for practices serving less deprived areas to have higher referral rates was no longer found where community clinics were held This is consistent with an interpretation that the provision of clinic appointments nearer to the homes of more socially deprived women and staffed by nurses results in GPs more likely to refer and/or women being more willing to attend these clinics than more distant regional clinics staffed by consultants. In addition, GPs commented that women were less likely to default from appointments at community clinics.

Genetic testing We found that the interaction with the GP was associated with an inappropriate level of interest in and expectation of the appropriateness of genetic testing, with 90% of those who had received information from their GP considering it important or very important compared to 73% of those who had not received information from their GP. While it is possible that this was due to recall bias, we consider this unlikely and suggest that this is worthy of further investigation. Since genetic testing is only appropriate to a very small percentage of women with very high familial risk, it is important that GPs do not foster this level of expectation.

This mismatch in perception about the role of molecular testing between those running cancer genetics clinics and women attending them may need to be addressed specifically in the way clinics are organised in the future and in postgraduate training of GPs.

Views of GPs on new services and on their role in cancer genetics

In general, GPs were confident about taking a family history, clinical examination and offering emotional support. They were less confident about risk assessment and deciding if mammographic screening was necessary, and most did not see it as their role to identify those from their lists who might be eligible for genetic counselling. Several commented that they and their staff did not have time to take on additional work of this nature.

There were no marked differences between the two trial groups suggesting that the limited number of contacts between the GPs and the genetics nurses who staffed the community clinics were insufficient to alter GP confidence in the management of these women. This was reinforced by the written comments of a number of GPs on the survey questionnaire that they had made little use of the service (the average referral rate was 0.5 referrals per GP per year). It has been noted previously that the limited interaction between primary care and specialist staff jeopardises achievement of one of the central aims of these initiatives – to facilitate integration and overcome barriers between primary and secondary/tertiary care (Bailey *et al*, 1994).

In general, GPs were positive about their patients being seen by genetic nurse specialists and about genetic clinics in the community. However, one-half still favoured hospital-based rather than locality clinics. General practitioners found the structured summary letter the most useful aspect followed by the provision of local community-based clinics. Most GPs regarded the referral guidelines provided by the study as useful. Other items (practice talks given by genetics nurse specialists, telephone advice and trial newsletters) were rated as useful or very useful by less than a third of the GPs.

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Appendix 4

Cross-sectional survey to estimate the prevalence of family history of colorectal, breast and ovarian cancer

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Short Communication

A cross-sectional survey to estimate the prevalence of family history of colorectal, breast and ovarian cancer in a Scottish general practice population

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A cross-sectional survey of all patients aged 30–65 in four general practices within one Local Health Care Co-operative in Fife, Scotland was undertaken to measure the prevalence of family history of colorectal, breast and ovarian cancer. A total of 7619 patients aged 30–65 responded to a postal questionnaire (response rate 59%). In all, 17% of respondents (1324, 95% CI 16–18%) reported a relative affected by colorectal, breast or ovarian cancer. Of those, 6% (78, 95% CI 5–7%) met the Scottish guidelines for referral for genetics counselling. In all, 2% (24, 95% CI 1–3%) of all individuals with an affected relative had received genetic counselling and risk assessment. Of these, 25% (6, 95% CI 8–42%) met the moderate- or high-risk criteria for developing a cancer. In conclusion, the number of patients who are at a significantly increased risk of cancer on the basis of a family history is small (approximately 10 per General Practitioner (GP) list). It is therefore unrealistic to expect GPs to develop expertise in genetic risk estimation. A simple family history chart or pedigree is one way that a GP can, within the constraints of a GP consultation, determine which patients should be reassured and which referred to the local cancer genetic clinic.
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Keywords: cross-sectional; family cancer history; genetic risk; prevalence

Cancer is one of the three health priorities of the National Health Service in Scotland (NHSiS) (Scottish Office, 1998). Local Health Care Co-operatives (LHCCs) were created in Scotland in 1998 to provide local management of services, and are made up of representatives of local general practices and local service groups and patient groups (Scottish Office, 1998). They have been charged with measuring health needs within their communities to reflect the clinical priorities for the area and to support the development of population-wide approaches to health improvement and disease prevention (Scottish Office, 1997).

Cancer genetics is the fastest growing area of clinical genetics (Wonderling *et al*, 2001). In Scotland, the four Regional Genetic Centres co-ordinate accurate risk assessment to ensure that individuals referred for screening investigations such as mammography and colonoscopy fulfil the national criteria laid down by the Cancer Genetic subgroup of the Scottish Cancer Group (Table 1). The lifetime risks for breast, colon and ovarian cancers in the general population are approximately one in 10, one in 60 and one in 90, respectively (ISD, 1998). All general practitioners (GPs) will, therefore, have patients with a relative with one of these cancers. An unknown proportion of these patients are likely to seek counselling and advice regarding their risk of developing cancer (Biesecker *et al*, 1993). The relative risk associated with a family history of these cancers has been widely reported (St John *et al*, 1993; Slattery and Kerber, 1994; Pharoah *et al*, 1997). The challenge is to identify the minority at significantly increased genetic risk of developing cancer while reassuring the majority whose family history does not indicate a likely increased cancer risk above that of the general population.

A major problem in planning cancer genetic services is that it is not known as to what proportion of the population fit into the various cancer genetic risk categories. The Scottish Office report 'Cancer Genetics Services in Scotland' (Haites, 2000) recognised that 'at present there is no means of identifying the total population who have a family history which places them at a significantly increased risk of developing breast, colorectal or ovarian cancer'. The report also noted that the uncertainty of these estimates makes it impossible to predict future costs for the provision of a risk estimation and screening service.

Risk estimation is based on the number of affected individuals within the family, the pattern of cancers and the age of onset of cancer. It is therefore necessary for the clinician to take a careful family history. This process is time-consuming and many GPs are unsure of their ability to obtain an accurate family tree and assess genetic risk (Fry *et al*, 1999). Pre-clinical family history questionnaires have been used extensively by genetic departments. This study was designed to evaluate how a similar questionnaire would be addressed by a general practice population and whether such a questionnaire might provide data in a form to facilitate GP cancer genetic risk estimation.

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Table 1 The Cancer Genetic Sub-committee family history criteria for enrolment in a screening programme for breast, ovarian or colorectal cancer

Breast
Moderate risk
One first-degree relative with bilateral breast cancer
One first-degree relative with breast cancer diagnosed under age 40 years or one first-degree male relative with breast cancer diagnosed at any age
Two first- or first- and second-degree relatives with breast cancer diagnosed under age 60 years and/or ovarian cancer at any age on the same side of the family
Three first- or second-degree relatives with breast or ovarian cancer on the same side of the family (always one first-degree relative unless history is via father)
High risk
An individual with BRCA1 or BRCA2 mutations or other known predisposing gene mutations or the untested first-degree relative of a mutation carrier
One first-degree relative (or second-degree relative via intervening male relative) in a family with four or more relatives affected with breast cancer or ovarian cancer in three generations
One first-degree relative (or second degree via father) with breast and ovarian cancer
Ovarian
Moderate risk
Two or more first- or first- and second-degree relatives with ovarian cancer
Two first- or first- and second-degree relatives with ovarian cancer at any age and breast cancer diagnosed under 50 years
One ovarian cancer and two breast cancers diagnosed less than 60 years on the same side of the family in first-degree relatives or second degree via a male
Two first- or second-degree relatives with colorectal cancer and/or endometrial cancer and one with ovarian cancer one affected relative with ovarian cancer and HNPCC family history
High risk
An individual with BRCA1 or BRCA2 mutations or other known predisposing gene mutations or her untested female relatives.
First-degree relative with breast and ovarian cancer
Bowel
Moderate risk
One first-degree relative with colorectal cancer under age 45 years
Two individuals affected with colorectal cancer (one less than 55 years) who are first-degree relatives of each other and one a first-degree relative of the consultant
Three affected family members with colorectal or endometrial cancer who are first-degree relatives of each other and one a first-degree relative of the consultant
High risk
An individual with a mutation in one of the mismatch repair genes or their untested first-degree relatives
A family history compatible with HNPCC according to Amsterdam or modified Amsterdam criteria

Individuals are judged to be at low risk if their family history does not meet the moderate risk criteria for screening.

We report the results of a cross-sectional survey conducted between May 1999 and October 2000 of patients in General Practice aged between 30 and 65 years to assess the prevalence of a significant family history of colorectal, breast, or ovarian cancer and to identify the number of individuals with a family history that had been referred onto the Clinical Genetic Service. Ethical approval for the study was granted by the Fife Local Research Ethics Committee.

PARTICIPANTS AND METHODS

A postal survey of all patients aged 30–65 years from four general medical practices covering over 99% of the population within one LHCC in Fife, Scotland was undertaken using a cancer family history questionnaire that had been developed and evaluated by a Cambridge-based research team (Leggat *et al*, 1999). The questionnaire was adapted to determine whether the patients had any concerns regarding their own risk of developing cancer and, if so, whether they had ever been referred to a cancer genetic specialist or had received any form of genetic counselling (questionnaire available online at http://137.195.14.43/cgi-bin/WebObjects/genisys.woa/wa/showDoc?docid = 208).

Patients were asked if they had any family members (grandparents, aunts, uncles, father, mother, brothers, sisters and children) who had had colorectal, breast or ovarian cancer and the age at which these cancers were diagnosed. Those with no affected relatives were requested to return the questionnaire at this point. Those with a family member affected were asked to complete a detailed family history including relationship to the affected individual, site of cancer and age at and date of diagnosis. In all, 305 randomly selected participants reporting a family history of cancer (23% of total) were interviewed by telephone ($n = 254$) or in person by a genetic nurse ($n = 51$) to check the consistency of the information collected via the postal survey. A fieldworker telephoned 101 of those reporting no family history to confirm that there was no family history of colorectal breast or ovarian cancer in their families.

RESULTS

A total of 13 155 questionnaires were mailed, of which 5535 were excluded from the study; 281 were returned address unknown and 5254 were not returned by the patient. In all, 7620 (3386 males, 4234 females) were completed and returned (Figure 1). The overall response rate was 59%. A total of 1396 (18%, 95% CI 17–19%) responders reported a family history of cancer. When checked by a genetics nurse, 72 questionnaires reported relatives with a history of cancers at other sites and were excluded from any further analysis. In all, 17% of respondents (1324, 95% CI 16–18%) therefore identified themselves as having a history of colorectal, breast, or ovarian cancer in a first- or second-degree relative. Of these, 918 were females and 375 males. Some respondents reported a family history of more than one of these cancers. In total, 78 respondents with a family history were classified as being at medium or high risk of developing colorectal, breast, or ovarian cancer, and thus met the guidelines for referral to cancer genetics services in Scotland for risk assessment (Haites, 2000). This represents approximately 6% (95% CI 5–7%) of all respondents reporting a family history of cancer.

Colorectal cancer

In all, 31 respondents reporting a family history of colorectal cancer met the national guidelines for referral for risk assessment, 11 males and 20 females, that is, 5% (95% CI 3–7%) of those reporting a family history of colorectal cancer and 2% (95% CI 1–3%) reporting a history of any of the three cancers or 0.41% (95% CI 0.26–0.55%) of the population surveyed.

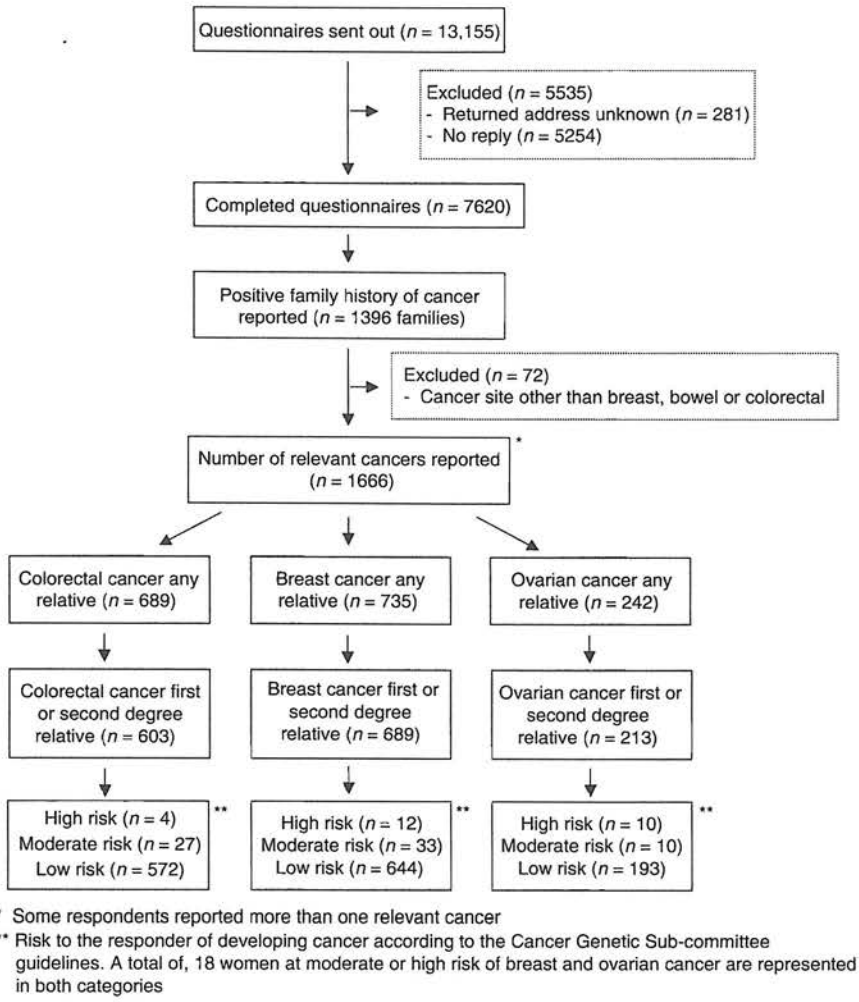

Figure 1 Flow diagram of response and results of a survey to estimate the prevalence of a family history of selected cancers in a Scottish population surveyed in 1999–2000.

Breast cancer

In all, 27 of the female respondents met national guidelines for referral for risk assessment for breast cancer only, that is, 3% (95% CI 2–4%) of all female respondents reporting a family history of cancer or 0.64% (95% CI 0.40–0.88%) of the total female population surveyed.

Ovarian cancer

Two female respondents met the national guidelines for referral for risk assessment for ovarian cancer only, that is, 0.2% (95% CI 0–0.5%) of all females reporting a family history of cancer or 0.05% (95% CI 0–0.1%) of the total female population surveyed.

Breast and ovarian cancer

In all, 18 female respondents met the national guidelines for referral for risk assessment, that is, 2% (95% CI 1–3%) of all female respondents reporting a family history of cancer or 0.43% (95% CI 0.22–0.62%) of the total female population surveyed.

Interviews of re-contacted participants

A validation study was undertaken in order to assess the consistency of this information. In all, 352 patients reporting a family history of cancer were randomly selected and asked to discuss their history with a genetic nurse either face to face or by telephone. Of these, 305 (87%) responded and their family history was verbally confirmed. Of these, 17 (6%, 95% CI 3–8%) were assessed to be at a moderate to high risk of developing colorectal cancer and thus met the national criteria for referral for risk assessment, 28 (9%, 98% CI 6–12%) met the referral criteria for breast cancer and three (1%, 95% CI 0–2%) for ovarian cancer.

As a result of this group being interviewed by the genetic nurse, the risk of 21 (7%, 95% CI 4–10%) of the respondents was altered. The estimated risk of one or more of the three cancers was increased for 16 of the respondents, although in six cases it was difficult to verify the risk due to incomplete information, for example, age of diagnosis of cancer in relative. For five respondents, the estimated risk of cancer was reduced. Only four (4%, 95% CI 0.2–8%) of the 101 respondents who originally reported no family history of breast, ovarian or colorectal cancer in the family history form subsequently mentioned a family history on interview with a fieldworker. All four were assessed to be at low risk of developing cancer.

Contact with health services

In all, 15% of respondents who reported a positive family history of these cancers had discussed their concerns with their GP, the great majority during the last 3 years. Out of these respondents, 86% (and 87% of the 30 respondents found to be at moderate or high risk) had raised the issue themselves (rather than their GP asking them about the family history of cancer). In all, 10% of respondents reporting any family history of cancer (and 22% of those at moderate/high risk) had been referred to a specialist to discuss their risk of cancer and 2% (25% of those at moderate/high risk) had received genetic counselling in the past.

Workload implications for GPs and cancer genetics clinics

Using these results to estimate workload for GPs and cancer genetic clinics in the rest of Scotland, the following figures are obtained:

Average caseload of a Scottish GP – 1700 patients
Average number of patients aged 30–65 years – 830 patients
Number with any positive family history (estimate) – 140 patients
Number who had discussed family history with GP – 21 patients
Number meeting referral guidelines (estimate) – 10 patients

Potentially, only one in 14 patients attending a GP with a positive family history of cancer needs to be referred to regional cancer genetics services for further risk assessment.

DISCUSSION

A valid response rate of 59% was achieved for the postal questionnaire used in this study. This is considerably higher than that in a previously published study using a similar questionnaire where the response rate was 29% (Leggat *et al*, 1999). Possible explanations for this high response rate to the questionnaire include: the study was led by the principal GP of one of the participating general practices and was thus well known to most patients; a press release publicising the study was issued prior to mailing; one reminder was sent out to nonresponders 2 weeks after mailing the questionnaire; and a colorectal cancer screening study had recently been undertaken in one of the four participating GP practices. When compared with the nonresponders, the responders were significantly older (mean age 48 years *vs* 44 years), similar to that reported in the previous study which evaluated the family history of cancer questionnaire.[9] The study made no allowance for multiple sampling of the same family, but the aim was to assess the burden of cancer genetics in a GP practice. Males with a family history of breast or ovarian cancer were assessed as low risk, as no clinical screening is indicated for them.

We have recently shown in Scotland that such reports of a positive family history of cancer are rarely incorrect but may substantially underestimate the true prevalence of a history of cancer in relatives, especially among second-degree relatives, when compared to cancer registry records (Mitchell *et al*, 2004). We only attempted to 'validate' a sample of positive reports of family history of cancer in this study. It is likely that a study which also involved an analysis of cancer registry records of all relatives would yield a higher estimate for the family history of cancer. Thus, the prevalence of family history of cancer in this study can be considered to represent a minimum estimate. Nevertheless, patients make decisions about seeking advice about their cancer risk based on their family history as they perceive it and so that data presented in this report are important in seeking to plan services for these patients.

It is interesting to note the higher incidence of moderate- or high-risk family histories in the subgroup of participants that agreed to be interviewed. This may reflect a greater interest in discussing their situation in the moderate- and high-risk groups.

Prior to the study, it was anticipated that some respondents might experience anxiety concerning their own risk of cancer as a result of completing the family history questionnaire. Participants were invited to voice their anxieties by phone with the study team who could then arrange an appointment with a genetic nurse. However, it was only necessary for the genetic nurse to contact two respondents in relation to this issue and she was able to provide advice and reassurance in both cases. Discussion with GPs in the practices involved revealed no contact with patients worried by the results of the study. Many of the respondents did admit to worries about their family history when interviewed, but had not taken advantage of genetic counselling. In fact, those at the greatest risk were the ones who reported least use of the service.

The majority of questionnaires were completed correctly and many respondents included a great deal of information about their family history of cancer, sometimes involving obtaining details from family members living abroad. For GPs faced with patients consulting with concerns about their family history, a suitable response would therefore be to ask the patient to complete a similar family history form and to rely on this in making a decision as to whether or not to refer the patient to the local cancer genetics clinic.

Cancer genetics referral guidelines are quite complex. Therefore, computer programmes have been developed based on referral guidelines to support the decision-making by GPs. However, as GPs will see only a few patients a year, acquiring all of the skills necessary for genetic counselling or to operate such programmes may be unlikely to be accorded a high priority. In addition, newly acquired skills following training are likely to degrade over time without frequent reinforcement. We suggest that GPs could use a questionnaire to collect information and then pass it on to the local genetic nurse, primary care genetic clinician or cancer centre for a rapid assessment as to whether further action should be taken.

The number of patients seeking genetic counselling has increased sharply over the last few years (Wonderling *et al*, 2001). This study has shown that only about one in 14 patients attending a GP with a positive family history of cancer needs to be referred to regional cancer genetics services for further risk assessment. The importance of the gate-keeping role of the GP is likely to increase in future. Our experience gained during the course of this study suggests that this role might be facilitated by the use of a self-completion family history form in general practice. Information collected by this means tallies closely with that obtained from interviews with trained genetic nurses and permit accurate risk assessments which can guide referral decisions.

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Appendix 5

Referrals of patients to colorectal cancer genetic services in South East Scotland

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Referrals of patients to colorectal cancer genetics services in south-east Scotland

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Key words: cancer, colorectal, expectation, genetic counselling, satisfaction

Abstract

The discovery that genetic factors are involved in the aetiology of colorectal cancer, has prompted many relatives of affected individuals to seek genetic counselling and screening. This paper describes the demand for genetic services by families with colorectal cancer in south-east Scotland, their expectations and views of the service offered. The annual referral rate over the 21-month study period, for patients with a family history of colorectal cancer, was 0.11 per 1000 patients on general practitioner lists. This is one third of the rate for patients with a family history of breast cancer and in comparison with the breast cancer group, relatives of colorectal cancer patients were significantly older and less socially deprived. Approximately one third were referred via a hospital specialist unit. One hundred patients were included in the study. Mean (± standard deviation) age was 43 (± 10.7 years), 75 were female and 31 were self referrals. Before the consultation, almost half the patients had an inflated perception of their risk and there was little change at follow-up. There was an improvement in objective understanding after counselling which was sustained up to 6 months but only two thirds remembered their objective risk accurately. Most patients were satisfied with the consultation. Our findings suggest the need to educate individuals, in particular men, younger people and the more socially deprived, about the relevance of a family history of colorectal cancer and to facilitate patients' comprehension of their risk status.

Introduction

Both genetic and environmental factors e.g. diet and exercise, influence the probability that an individual will develop colorectal cancer (CRC). A significant minority of CRC cases result from two autosomal dominant syndromes – familial adenomatous polyposis (FAP) and hereditary non-polyposis colon cancer (HNPCC). Other less understood genetic factors are also likely to be involved in CRC and may account for 15% of cases [1].

Media attention to these discoveries has led many individuals with a family history of CRC to seek genetic counselling and advice about screening. Petersen et al. [2] and Trimbath and Giardiello [1] have stressed the importance of providing genetic counselling for individuals in families with CRC who wish risk assessment. They list the main components of the counselling session e.g. construction of a family pedigree, education of the patient and family about medical aspects of the disorder, risk and screening and exploration of psychological factors such as specific issues related to the family history and experience of the disorder.

Wonderling et al. [3] found that in Scotland the annual referral rate to cancer genetics services was 278 per million population. In the whole of the UK 18% of these referrals had a family history of CRC. Several studies have been made of genetic services offered to relatives of CRC patients but these have often been focussed on attitudes to and outcomes of genetic testing [e.g. 4, 5, 6, 7]. There have been few studies evaluating other aspects of familial CRC services. Amongst these Collins et al. [8, 9] assessed a familial CRC clinic and

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Julian-Reynier et al. [10] and Nordin et al. [11] assessed clinics for patients with a family history of CRC or other cancers.

We therefore carried out a survey of patients presenting with a family history of CRC in Scotland in order to inform the development of appropriate services. We investigated the referral rate to the Clinical Genetics Service and patients' referral pathways. We also studied sociodemographic and psychological characteristics of patients, their knowledge and information requirements. Finally, we measured patient satisfaction with the service received, information retained and further action taken by patients after the consultation.

We have recently reported our experience in managing patients with a family history of breast cancer [12, 13, 14] and these results will be compared with current findings.

Materials and methods

Procedure

Ethical approval for the study was obtained from the local ethics committee. A total of 203 GP practices in south-east Scotland (Lothian, Borders and south-west Fife regions) were invited, by letter, to take part in the study. Some 170 (84%) agreed, 23 (11%) declined and 10 (5%) did not reply.

During the study period (1 March 1998 to 30 November 1999), referrals of patients with a family history of CRC, from participating practices, were sent to the regional Clinical Genetics Service at the Western General Hospital. Some referrals were sent directly by the GP and others were sent to a hospital gastrointestinal unit and re-referred from there. Patients resident outside south-east Scotland and those known to be symptomatic or to have been diagnosed with CRC were excluded from the study. Those known to have previously consulted another clinic about their family history of cancer or whose family was already known to the Clinical Genetics Service, were also excluded.

All eligible patients were sent a letter giving details of the study and were asked to complete a consent form. Those who agreed to take part in the study were sent a baseline questionnaire. On receipt of the completed baseline questionnaire all patients were offered a clinic appointment with a consultant geneticist/specialist registrar or a specialist genetic nurse. Patients were seen either in one of four hospital outpatient departments or in a community clinic based in a general practitioner (GP) surgery. At the clinic appointment details of the family history were obtained. Amsterdam II criteria [1] were used to identify patients at high risk, in families with HNPCC. Patients were estimated to be at moderate risk if their family history satisfied published criteria [15]: i.e. one first degree relative diagnosed with CRC under 45 years or two first degree relatives with CRC on the same side of the family. Patients not in the high or moderate risk categories were considered to be at low risk: defined as the same or slightly higher than the general population risk. Patients at low risk were reassured that no screening was necessary and discharged. Patients at high and moderate risk were referred for colonoscopy if appropriate. Immediately after the consultation patients were sent a letter summarising the matters discussed. Follow-up questionnaires were sent to all patients 4 weeks and 6 months after the appointment. For the purpose of the present study we did not collect data relating to patient management, following referral to other hospitals for possible colonoscopy.

Patients who were excluded or who did not consent to take part received the same service as those in the study but did not receive any questionnaires.

Referrals

The total number of referrals of patients with a family history of CRC, from all 203 practices invited to take part, during the 21 month period of the study was recorded. The total number of patients on the lists of all these practices was 1,221,261 at the beginning of the study period. The absolute annual referral rate was estimated as:

$$(\text{total referrals per year}) \times 1000/(\text{total list size for all practices})$$

Age, gender and source of referral were recorded for all patients from participating GP practices. The Carstairs deprivation score (CDS), which is based on postcode of residence, was used as a measure of social deprivation [16]. The range of this score for all postcodes in Scotland was −7.54–12.87 with higher positive scores indicating greater social deprivation.

Participants

Sociodemographic characteristics

Several sociodemographic characteristics of patients were assessed at baseline including age, gender, marital status, education and CDS.

Mode of referral

Patients were asked if they had taken the first step in asking to be referred (self referrals) or if this had been suggested to them by a medical professional (other referrals).

Psychological measures

Perceived risk of CRC. Patients were asked to state whether they considered their risk to be high, moderate or low. They were also asked to categorise their risk in terms of the general population risk (lower, same, slightly higher, much higher) and the number of times their risk of ever developing CRC was greater than that of the average person.

Cancer Worry Scale (CWS) (Watson et al. [17]). This 6 item, self-report scale (adapted from 4 single items,

Lerman et al. [18, 19]) assesses concerns about developing cancer and their impact on daily functioning. Total scores range from 6 to 24 where a higher score indicates higher levels of worry. The psychometric properties of the scale have been shown to be satisfactory [20, 21].

Subjective understanding. Patients were asked to rate on a 4-point scale from 1 (*not at all*) to 4 (*very well*) how well they understood each of 4 issues relating to CRC genetic risk. The issues were:

1. How increased risk of developing CRC can be passed on in families.
2. The significance of their own family history of cancer.
3. Whether there is anything people can do for themselves to reduce their risk of developing CRC.
4. What services may be offered to protect the health of people at increased risk of developing CRC.

Responses were summed to give a composite score for subjective understanding ranging from 4 to 16.

Objective understanding. Patients were asked to consider a number of factual statements and to respond 'true', 'false' or 'don't know'. There were 10 statements about CRC genetics (e.g. most cases of CRC are caused by inheriting a faulty gene) and 10 about issues to do with CRC symptoms and screening (e.g. symptoms which may be associated with early CRC are blood in the stools). A correct response was scored as '1' and 'incorrect' or 'don't know' as zero to give total scores for objective understanding of genetics and of CRC/screening from 1–10.

Information and services required
Patients were asked at baseline how detailed was the information they required from the consultation. They were also asked to rate how important it was for them to get information about specific items such as risks, prevention, screening and treatment. Questions were also asked about their desire for access to various forms of screening.

Clinic consultation
Details of all clinic consultations were recorded. These included matters discussed, duration of consultation, level of stated risk, and outcome of the consultation.

General satisfaction
At the 4-week and 6-month follow-up, satisfaction with the consultations was measured in several ways. To assess general satisfaction, patients were asked to state their views on a number of aspects of the service which were derived or adapted from the Medical Interview Satisfaction Scale (MISS) (Wolf et al. [22]). Satisfaction with three aspects of a consultation was measured:

1. The affective aspect (A) – the extent to which patients felt that the medical professional listened, understood and was interested.
2. The behavioural aspect (B) – the patient's evaluation of the medical professional's competence in the consultation.
3. The cognitive aspect (C) – satisfaction with the amount and quality of information provided by the medical professional.

Each item on the scale was rated on a five point scale of agreement from 5 (strongly agree) to 1 (strongly disagree). Items l, n, p and q (see Table 3) were scored in the reverse direction.

For those patients who responded to all the items in a group (A, B or C) a mean score was calculated for the group of items. An overall mean satisfaction score was also calculated for those who had responded to all 17 questions.

Specific satisfaction
We investigated patients' assessment of the helpfulness of specific information given about genetic risks, symptoms of CRC, screening and treatment and of services offered for screening and treatment.

Recall of risk
Four weeks and 6-months after counselling, patients were asked to state their level of risk of developing CRC, given at the clinic appointment. This was compared with the objective risk stated by the medical professional.

Additional information/services
Patients were asked if there were other topics they would have liked to have discussed at the clinic or other services they would have liked to have been offered. We also investigated whether patients intended to or had sought further information after their clinic appointment from any source.

Statistical methods
Descriptive statistics were generated to describe the study population. Differences between two independent groups were analysed, with parametric or non parametric tests as appropriate, using the independent samples *t*-test (2 tailed), Mann–Whitney (2 tailed), chi-squared (2 tailed) or Fisher's exact test (2 tailed). The Kruskal–Wallis test was used to test for differences between more than two independent group. Differences between pairs of observations in the same group were analysed using the paired *t*-test (2 tailed). The Pearson correlation coefficient or the Spearman–Rank correlation coefficient was used to test for associations between two variables.

When multiple comparisons were made between groups the Bonferroni correction was used when assessing statistical significance.

If one or more scores on a scale were missing the total score for that patient was not included in any statistical analysis. When considering information required from the consultation and helpfulness of information given,

patients with different categories of response were combined into one group if numbers were small.

A significance level of 0.05 was used throughout. The data was analysed using SPSS for Windows, version 9.

Results

Referrals

The absolute annual referral rate (and 95% confidence interval) per 1000 patients on the GP lists was 0.11 (0.09–0.13) during the study period.

A total of 150 patients, over a 21-month period, were invited to participate. Of these, 93 (62%) were referred directly by their GP and 52 (35%) via a hospital gastrointestinal unit. The remaining 5 patients were referred from a variety of sources. A total of 107 (71%) were female and 43 male. The mean (standard deviation) of age and CDS were 42.1 years (11.0 years) and −1.9 (3.0), respectively.

Participants

Figure 1 shows patient participation and completion of questionnaires. A total of 100 (67%) patients were included in the study. No significant differences in sex distribution, age or CDS were found between these patients and the 50 who did not take part. Of patients sent the 4 week questionnaire a total of 79 (92%) completed it. The corresponding figure for the 6-month questionnaire was 78 (87%).

Sociodemographic characteristics

Sociodemographic characteristics of patients who completed the baseline, 4-week and 6-month questionnaires are summarised in Table 1. There were no significant differences in sociodemographic characteristics or baseline psychological measures between the patients who did/did not complete the 4-week or the 6-month questionnaires.

Mode of referral

Thirty-one (31.3%) patients who responded said they were self referrals. Of these, 17 (63%) who responded indicated it was their own concern and almost all the others requested referral at the suggestion of another family member. Of those who stated that they were 'other referrals' ($n = 68$), the number of patients stating that they had specifically enquired about their family history of cancer was 37 (57%). For 19 (28%) the suggestion of referral had taken place when they had seen the doctor about another matter.

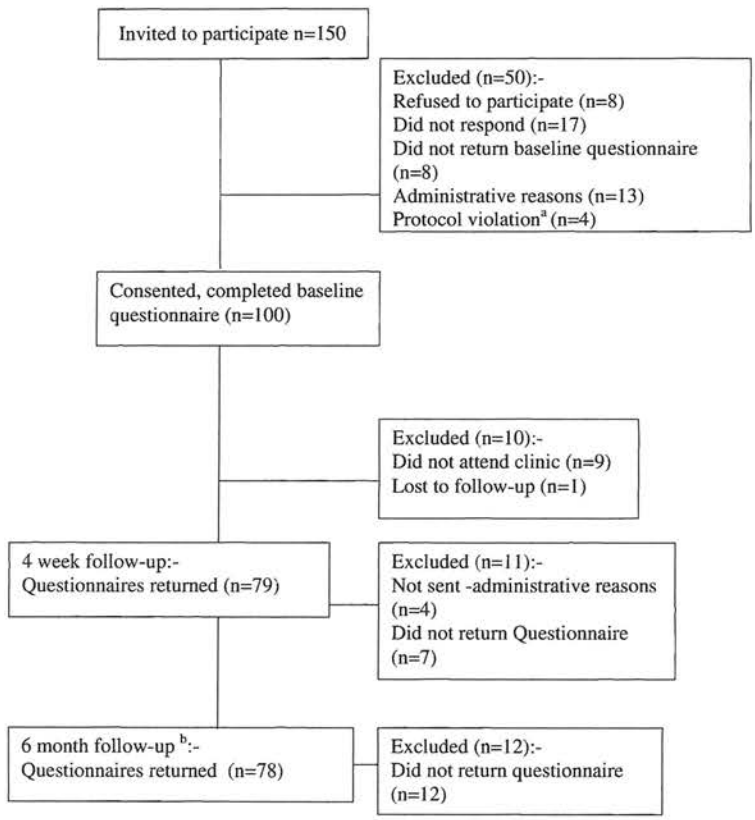

Figure 1. Progress of participants through the study.
[a]E.g. the patient had received genetic counselling elsewhere or had been treated for cancer.
[b]Seven patients who were excluded in the 4-week follow-up were included at the 6-month follow-up.

Table 1. Sociodemographic and psychological characteristics of patients at baseline and 4-week and 6-month follow-up.

Variable	Baseline (n = 100)	4 Weeks (n = 79)	6 Months (n = 78)
Sex: n (%)			
Male	25 (25)	22 (28)	19 (24)
Female	75 (75)	57 (72)	59 (76)
Marital status: n (%)			
Married/cohabiting	76 (76)	60 (76)	58 (74)
Separated/divorced/widowed	8 (8)	6 (8)	7 (9)
Never married	16 (16)	13 (16)	13 (17)
Education: n (%)			
To age 16 years	31 (31)	25 (32)	24 (31)
To age 18 years	10 (10)	8 (10)	7 (9)
After age 18 years	22 (22)	17 (21)	16 (20)
University graduate	37 (37)	29 (37)	31 (40)
Age (years): mean (s.d.)	43.0 (10.7)	43.7 (10.6)	44.1 (11.2)
Carstairs deprivation score: mean (s.d.)	−2.2 (2.9)	−2.2 (2.8)	−2.3 (2.8)
Risk of CRC: n (%)			
Objective:			
Low	45 (47)	38 (48)	35 (45)
Moderate	44 (45)	34 (43)	35 (45)
High	8 (8)	7 (9)	8 (10)
Perceived:			
Low	5 (5)	8 (11)	9 (14)
Moderate	59 (60)	56 (76)	46 (71)
High	35 (35)	10 (13)	10 (15)
Understanding: median (inter-quartile range)			
Subjective	9 (7–11)	12 (11–15)	12 (11–14)
Objective:			
Genetics	4 (2–7)	7 (5–8)	7 (5–8)
Symptoms/screening	6 (4–8)	8 (6–9)	9 (8–9)
Cancer worry scale: mean (s.d.)	10.8 (3.0)	9.9 (2.7)	10.1 (2.9)

There were no statistically significant relationships between mode of referral (self/other) and age or sex. Similarly there were no significant differences between the proportions with different modes of referral in the 4 educational classes. However there was a greater tendency for those with more education to be self referrals. Of those who had left school at 16 years, 19% were self referrals, compared with 44% of University graduates. There was a highly significant ($P < 0.001$) difference in deprivation as measured by CDS ($P < 0.001$) between patients in the self and other referral groups. Only 20% of the more deprived patients (CDS ≥ overall mean) were self referrals compared with 43% of the less deprived patients (CDS < overall mean).

Psychological characteristics

Perceived risk of CRC. At baseline 95% patients perceived their risk of developing CRC to be high/moderate (Table 1). By the 6-month follow-up the percentage had reduced to 86%. Considering only the 56 patients who had completed all 3 questionnaires, 29 (52%) were at high/moderate objective risk and the percentages who perceived their risk to be high/moderate were 91%, 86% and 86% at baseline, 4-week follow-up and 6-month follow-up, respectively.

Amongst patients who perceived their risk to be high/moderate 56 (62%) at baseline, 33 (50%) at the 4-week follow-up and 28 (49%) at the 6-month follow-up considered that their risk of developing CRC was at least 5 times greater than the average person. However, the majority [65 (94%) at baseline, 58 (87%) at the 4-week follow-up and 48 (83%) at the 6-month follow-up] of patients who considered their risk to be the same or slightly higher than the general population perceived their risk to be high/moderate.

Cancer Worry Scale. Mean scores on the Cancer Worry Scale at the different time periods are given in Table 1. Changes in the scores over time were measured in the 59 patients for whom there was a baseline, 4-week and 6-month measurement. There was a highly significant ($P < 0.001$) decrease in score between baseline and the 4-week questionnaire but not between the 4-week and 6-month questionnaire. The results were identical when patients at high/moderate (n = 32) and low risk (n = 27) were compared separately.

Subjective and objective understanding. Baseline: When patients were asked how well they understood the 4 issues relating to subjective understanding, the responses to questions 1–3 were similar with 11–15% stating they had no knowledge, 43–49% saying they had a little knowledge and 36–46% saying they had more than this. Patients had less knowledge of the services which could be offered to at risk individuals (question 4) with 36 (36%) stating that they had no knowledge and 36 (36%) that they had a little knowledge.

Median total scores for subjective and objective understanding are given in Table 1. There were significant correlations of 0.34 ($P < 0.01$) between subjective understanding and objective understanding of genetics, 0.35 ($P < 0.01$) between subjective understanding and objective understanding of CRC/screening and 0.54 ($P < 0.001$) between objective understanding of genetics and objective understanding of CRC/screening.

There were no significant differences in subjective understanding or objective understanding of genetics between patients of different sexes, age groups (<40 years, ≥ 40 years), mode of referral (self and other) groups and educational groups. At baseline there was one significant difference in objective understanding of CRC/screening with female patients having more knowledge than male patients ($P < 0.01$).

Changes over time: Changes in each of these scores were measured in the 56 patients for whom there was a baseline, 4-week and 6-month measurement. There were highly significant ($P < 0.001$) increases in subjective understanding and objective understanding of both genetics and of symptoms/screening, between baseline and the 4-week questionnaire but not between the 4 week and 6-month questionnaire. The results were identical when patients at high/moderate ($n = 29$) and low ($n = 27$) objective risk were compared separately.

Information and services required

Seventy-seven percent of patients said they would like as much information as possible but 8 patients (8%) wanted general information only and 14 patients (14%) only wished to know if their family was at increased risk. Patients in the first group had significantly higher scores on the Cancer Worry Scale than patients in the other two groups combined ($P < 0.05$).

Items of information which over 70% patients regarded as very important included their own risk of CRC, symptoms of CRC to look for and the pros and cons of colonoscopy. Services, which over 60% of patients regarded as very important included reassurance that they show no signs of cancer now, regular check-ups and the opportunity to take part in research to improve services for the future.

Clinic consultations

Of the 100 patients who were entered into the study, 9 did not attend their clinic appointments and for another 7 no record was kept of their appointment in error. Details were available for the other 84 consultations.

Matters discussed and duration of the consultation

Matters discussed at the consultation were classified under 4 headings:

1. Family history and genetics;
2. Examination and screening;
3. Healthy lifestyles;
4. Other matters related to bowel cancer.

The genetics of CRC, the significance of their family history and the patient's own risk, were discussed in over 95% of all consultations. In a large proportion (43–75%) of consultations there was also discussion of risks to children and other relatives, the possibility of finding a cancer predisposing gene and the risks of developing any other cancer.

Colonoscopy was discussed in 94% consultations. Screening by looking for blood in the stools (FOB test) and removal of bowel growths was discussed in 79% of consultations.

With regard to healthy lifestyles: dietary factors were discussed in 92% of consultations. Symptoms, which may be related to CRC, were discussed at 87% of consultations.

The median time for the whole consultation was 42 min with almost half of this time being taken up with a discussion of the family history and genetics.

Risk of developing CRC and outcome of consultation

Of the 82 patients in whom CRC risk was estimated, 45 (55%) were at high or moderate risk of developing CRC and 37 (45%) were at the same or slightly higher than the general population risk (low risk group). Amongst the high/moderate risk group colonoscopy was suggested for 93%. Over half of the low risk patients were advised of the possibility of FOB testing if they required further reassurance.

Given an annual referral rate of 0.11 per 1000 patients on GP lists and assuming that the risk distribution of all patients referred is the same as for the above 82 patients, we can estimate that there will be 0.06 new patients, per 1000 population in south-east Scotland, requiring colonoscopy surveillance per year.

General satisfaction

For all consultations, patient responses to the MISS items were heavily skewed towards the 'satisfied'. In Table 2, the views of all patients at the 4-week and 6-month follow-up are given. The items are listed along with the aspect of the consultation measured and the number and percentage of patients who agreed/strongly agreed with the statement (or disagreed/strongly disagreed-items l, n, p, q). Patients who did not respond to the question or who stated that the item was not applicable were not included. In general, most patients were satisfied with the consultations.

Table 2. Satisfaction with cancer genetics services: numbers and percentages of patients who agreed/strongly agreed[a] with various statements concerning their appointments at the 4-week and 6-month follow–up.

Statement	Aspect[b] of consultation	4-Week follow-up $n = 79$	6-Month follow-up $n = 78$
a) I was told about my risk of developing cancer in words that I could understand	C	69 (95.9%)	72 (93.6%)
b) After the consultation I have a good idea of what changes in my health I should seek medical advice about.	C	59 (86.8%)	63 (85.1%)
c) At the consultation I was told all I wanted to know about my family history of CRC	C	58 (80.5%)	56 (74.7%)
d) The person I saw was very good at explaining the reasons for any medical tests which may be necessary	C	67 (94.4%)	63 (88.7%)
e) I feel I understand pretty well the plan for helping me	C	59 (89.4%)	58 (81.7%)
f) I was given a chance to say what was really on my mind	A	67 (93.0%)	66 (86.9%)
g) I really felt I was understood	A	61 (85.9%)	61 (81.4%)
h) After the consultation I felt much better about my problems	A	48 (73.9%)	50 (68.5%)
i) I felt the person I saw really knew how upset I was about my family history	A	34 (66.7%)	40 (67.8%)
j) I felt free to talk about private thoughts	A	56 (83.6%)	59 (83.1%)
k) I felt accepted as a person	A	63 (91.3%)	66 (94.3%)
l) I felt that my problems were not taken seriously	A	59 (89.4%)	64 (86.4%)
m) All the problems I mentioned were looked into	B	49 (83.0%)	58 (87.9%)
n) I felt the person I saw did not spend enough time with me	B	66 (91.6%)	72 (92.3%)
o) I was satisfied with the advice I was given about the courses of action I could take.	B	60 (85.7%)	65 (85.5%)
p) The person I saw seemed rushed during the consultation	B	67 (91.8%)	73 (93.6%)
q) The person I saw gave me too much information too quickly	B	68 (93.1%)	66 (84.6%)

[a]Disagreed/strongly disagreed items l, n, p, q.

[b]Aspect of consultation: A – The affective aspect – the extent to which patients felt that the medical professional listened, understood and was interested; B – the behavioural aspect – the patient's evaluation of the medical professional's competence in the consultation; C – the cognitive aspect – satisfaction with the amount and quality of information provided by the medical professional.

Mean scores for items in groups A, B, and C and overall satisfaction scores at the 4-week and 6-month follow up are given in Table 3. There were no significant differences between the mean A, B, and C scores at the 4-week follow-up. However at the 6-month follow-up the B scores were found to be significantly greater than the A scores ($P < 0.05$). The magnitude of the difference was small but suggests a greater satisfaction with the medical professional's competence than their ability to empathise.

There was no significant difference in overall satisfaction score by sex, objective risk, education level, referral method or level of information requested by the patient. There was no significant correlation between overall satisfaction score at the 4-week follow-up and age or CDS.

Specific satisfaction

At the 4-week follow-up, over 85% of patients rated the information on the genetics of bowel cancer, the significance of the family history, their own risk and the pros and cons of colonoscopy as quite or very helpful. At the 6-month follow-up information on strategies to reduce cancer risk in everyday life, and symptoms of bowel cancer to look for were also rated in this way.

Recall of risk

Amongst the 71 patients who completed both questionnaires 37 (52%) were estimated to be at high or moderate risk of developing CRC and 34 (48%) to be at low risk. Table 4 gives the numbers and percentages of patients by level of risk recalled 4 weeks and 6 months after counselling. Only two thirds remembered their level of risk accurately.

Additional information/services

Only a minority (10%) of patients at follow-up reported that there were other topics which they would have liked to discuss at the clinic. At the 4-week follow-up 16 (20%) patients suggested additional services that they would

Table 3. Satisfaction with cancer genetics services (mean scores (± SD) for different aspects of the consultation at the 4-week and 6-month follow-up.

Score	4-Week follow-up	6-Month follow-up
Group A (affective)	4.04 ± 0.72	4.05 ± 0.66
Group B (behavioural)	4.24 ± 0.57	4.19 ± 0.50
Group C (cognitive)	4.22 ± 0.64	4.11 ± 0.59
Overall satisfaction	4.07 ± 0.62	4.13 ± 0.54

Table 4. Recall of risk 4-weeks and 6-months post counselling.

	Risk recalled		
High/moderate risk group (n = 37)			
Time interval	Correct	Low risk	Could not remember
4-Week follow-up	22(59%)	8 (22%)	7 (19%)
6-Month follow-up	26 (70%)	7 (19%)	4 (11%)
Low risk group (n = 34)			
Time interval	Correct	High/moderate risk	Could not remember
4-Week follow-up	22(65%)	9 (26%)	3 (9%)
6-Month follow-up	21 (62%)	10 (29%)	3 (9%)

like to receive. Nine of these patients noted their interest in genetic testing. There was no significant difference in the overall satisfaction score of the patients who wished further check-ups regarding their CRC status and patients who wanted other/no services. At the 6-month follow-up 18 (23%) patients suggested additional services. Six patients noted screening for other cancers, five screening by the FOB test and five genetic testing.

Further action since attending clinic(s)

At the 4-week follow-up 24 (34%) patients said they intended to seek further advice about their family history of cancer. At the 6-month follow-up only 10 (14%) had actually sought further information. There were no significant differences in overall satisfaction scores at the 4-week follow-up between patients who intended/did not intend to seek further advice or those who had/had not sought further information.

Discussion

The present study was carried out to assist in the development of genetic services for relatives of patients with CRC. We estimated demand for genetic services amongst relatives of CRC patients in south-east Scotland. We also considered mode of referral, sociodemographic and psychological characteristics of patients referred, prior views about the service they wished to receive and their satisfaction with the service offered.

Referrals

During the study, the annual referral rate for patients with a family history of CRC, was approximately one third of the referral rate for patients with a family history of breast cancer (0.31 per 1000 patients) in the same time period [13]. Since this was a population based study these figures can be applied to the population of south-east Scotland. From data given by Wonderling et al. [3] we can estimate that, in their study, the annual referral rate in Scotland of patients with a family history of CRC was 0.05 per 1000 population. This referral rate is less than half that found in the present study but assumes that the percentage of referrals with a family history of CRC was the same in Scotland as in the rest of the UK. In a recent study carried out in Scotland [23], 8% of participants reported a family history of CRC in at least one first or second degree relative whereas 52% of women had at least one first or second degree relative with breast cancer. Taking patients of both sexes together the ratio of those reporting a family history of breast cancer to those reporting a family history of CRC was 3 : 1. Therefore the ratio of referral rates which we found is in agreement with expectation. However as shown by Mitchell et al. [24] this ratio does not represent the true ratio of patients with a positive family history of these cancers since sensitivity of reporting a positive family history is much greater in breast than colorectal cancer.

One third of patients were referred via a hospital specialist unit compared with only 14.5% of patients seeking counselling regarding a family history of breast cancer [13]. Thus GPs are less likely to refer asymptomatic patients with a family history of CRC direct to cancer genetic services than those with a family history of breast cancer. At the start of the study GPs were issued with referral guidelines for patients with a family history of breast cancer and CRC. They also received biannual genetics update newsletters during the course of the study. However, after the study was completed over 40% of GPs who had taken part were at most only a little confident about deciding whether patients with a family history of breast cancer or CRC should be referred to genetic services [13]. This is probably also the explanation for the large proportion (47%) of CRC patients in the study who were at low risk.

Over two thirds of patients invited to participate were female. Wonderling et al. [3] found the same proportion amongst bowel cancer referrals to UK cancer genetic services. It was felt that this was due to the fact that men generally underuse health services.

The mean age of patients invited to participate was higher and the mean deprivation score lower than for patients referred with a family history of breast cancer in the same time period. This indicates that younger and more socially deprived individuals are less likely to be referred regarding a family history of CRC than that of breast cancer. This may be because fewer socially

deprived relatives of CRC patients seek advice and also because of ignorance of diagnoses of CRC in relatives.

One third of patients invited to take part did not do so. One half of these failed to return their consent form or baseline questionnaire. There was no evidence that these patients differed from those who took part in age, sex or social deprivation.

Participants

The mean age of patients included in the study was 43 years, 5 years older than for patients seen in the same time period with a family history of breast cancer [14]. This was probably due to greater media publicity regarding the risks associated with a positive family history of breast cancer compared to that for CRC. Women in the group with a positive family history of breast cancer were more likely to be self referrals who were younger than those referred by a medical professional [13]. In three other studies of patients attending cancer genetics clinics [8, 10, 11] a similar mean age was found to that in the present study.

Thirty one percent of participants were self referrals in contrast to 43% in the case of breast cancer [13]. Self referral rates were higher in less deprived and better educated groups. This is in contrast to the patients with a family history of breast cancer for whom no difference in deprivation score (CDS) was found between referral groups.

At baseline almost all the patients in the study perceived their risk of developing CRC to be moderate or high. Collins et al. [8] also found that many were coming to the clinic with inflated perceptions of their own risk.

Most patients stated at baseline that they had at least a little knowledge of CRC risk and preventive measures. Over one third had no knowledge of services which could be offered to protect the health of people at increased risk. However, the correlations between baseline subjective and objective understanding were relatively low suggesting that their perceived level of knowledge was often inaccurate. There was a suggestion that patients with more education had a better understanding of genetics and females had more knowledge of CRC and screening than males. Collins et al. [8] also found that increased education was associated with increased knowledge.

We found that over three quarters of the patients wanted to obtain as much information as possible at their consultation. These patients had higher baseline scores on the Cancer Worry Scale. Nordin et al. [11] found that patients they referred to as 'monitors', who sought more information, also had higher levels of cancer worry on a numerical 1–7 scale with end points defined as no worry at all and worst possible worry.

The items about which patients in our study were most concerned to get information were those concerned with their own risk and its possible reduction and early detection of CRC. Collins et al. [8] found that their patients were most concerned to find out if there was a gene for cancer in their family. This was not a major concern for patients in this study.

Many of our patients wanted to have an opportunity to take part in research. Collins et al. [8] found that helping research or science was an important motivation for attendance for over half of their participants.

Consultation

Almost half the patients were informed, at the consultation, that their risk was at most slightly higher than that in the general population. However, at follow-up the majority of patients perceived their risk to be high/moderate.

Most patients were satisfied with the consultation in general with satisfaction scores being very similar to those found for the breast cancer group [14]. We found no difference in satisfaction between certain patient groups. Collins et al. [9] found that older age group and lack of worry about CRC were associated with a high level of satisfaction. Nordin et al. [11] found that monitors were less satisfied with the information aspects of counselling compared with non monitors.

At follow-up only 60–70% patients estimated to be at high/moderate risk of developing CRC remembered their objective risk correctly and about 20% considered their risk to be low. Amongst the patients estimated to be at low risk 62–65% remembered their objective risk correctly but 26–29% recalled their risk to be high or moderate. There were similar findings in the study of Nordin et al. [11] where after counselling 25% overestimated their risk and 18% underestimated their risk. This indicates that some patients may not have understood the information about risk given to them at the clinic appointment and doctors/nurses may need to take more time to ensure patients understand their risk status and the resulting options open to them. Accuracy of recall of risk was unrelated to age, sex education or baseline cancer worry.

However, despite the above results, when asked about their perception of their risk over 85% patients stated it to be high/moderate at baseline and at the 2 follow-up times. This suggests that although some patients accept that their objective risk is low they still perceive themselves to be at higher risk. Similar results were found for relatives of breast cancer patients referred during the same time period [12]. This is in contrast to the results of Collins et al. [8], who found close agreement between subjective and objective risk after counselling. There were, however, highly significant increases in subjective and objective understanding after genetic counselling. Patients with a family history of breast cancer showed similar increases in understanding [12].

There was a reduction in score on the Cancer Worry Scale after counselling as was also found for relatives of breast cancer patients [12]. Other workers [17, 21, 25] have used the same Cancer Worry Scale as in

the present paper in studies of patients with a family history of breast cancer. These workers found very similar scores at baseline to those in the present study. In two of the studies [17, 25] there was a reduction in score after counselling as in the present study. Hopwood et al. [21] found no change and pointed out that it is important to identify those patients for whom such worries are intrusive and impair their day to day functioning rather than assume that all cancer worry is pathologic.

About 20% patients said they would have liked to have been offered access to services not offered to them at the clinic consultation. At the 4-week follow-up 34% patients said they intended to seek further advice about their family history of cancer but less than half this percentage had actually done so at the 6-month follow-up.

Limitations of the study

The results of this study are based on a relatively small number of patients all from the same region of south-east Scotland so should be treated with caution. Patients who did not consent to take part in the study did not differ from others in age sex or social deprivation but we did not have data on psychological characteristics Nevertheless, where it is possible to compare our results with those of others, as discussed above, the findings are very similar. Our patients were followed up for a comparatively short period of time and it would be interesting to investigate their views and actions over a longer period since their appointments.

Clinical/research implications

Our results would suggest the need to give GPs more information about the service offered to CRC families and to encourage them to refer directly to genetic services. There is also the need to encourage patients with CRC to inform relatives of the diagnosis, so that they can be offered screening if appropriate. At present male relatives and those from socially deprived areas are less likely to come forward for counselling and screening. There is a need to make counselling and screening more accessible to these relatives e.g. through the provision of clinics in GP surgeries [13]. Patient recall and perception of risk after counselling was poor and this suggests the need for some reinforcement of the information given as this is likely to influence attitudes to screening.

Conclusions

This study shows that families with CRC in south-east Scotland are generally satisfied with the service received. Although many patients did not remember or had an inaccurate perception of their level of risk up to 6-months after counselling, there was an increase in objective understanding and a decrease in cancer worry, after counselling. Our results indicate a need to target certain groups to educate them about the possibility of risk assessment and screening for CRC.

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Appendix 6

Dukes' Stage and TNM of colorectal tumour

Appendix 6

Modified Duke Staging System

Duke A The tumour penetrates into the mucosa of the bowel wall but no further

Duke B **B1**: tumour penetrates into, but not through the muscularis propria (the muscular layer) of the bowel wall.
B2: tumour penetrates into and through the muscularis propria of the bowel wall.

Duke C **C1:** tumour penetrates into, but not through the muscularis propria of the bowel wall; there is pathologic evidence of colon cancer in the lymph nodes.
C2: tumour penetrates into and through the muscularis propria of the bowel wall; there is pathologic evidence of colon cancer in the lymph nodes.

Duke D The tumour, which has spread beyond the confines of the lymph nodes (to organs such as the liver, lung or bone).

TNM Staging System (Tumour, Node, Metastasis)

Tumour

T1: Tumour invades submucosa.

T2: Tumour invades muscularis propria

.

T3: Tumour invades through the muscularis propria into the subserosa, or into the pericolic or perirectal tissues.

T4: Tumour directly invades other organs or structures, and/or perforates.

Node

N0: No regional lymph node metastasis.

N1: Metastasis in 1 to 3 regional lymph nodes.

N2: Metastasis in 4 or more regional lymph nodes.

The corresponding Dukes' classification of a tumour to the TNM classification.

TNM	Classification	(American joint commission on cancer)		Dukes' classification
Stages	T	N	M	Stages
Stage 0	Tis	N0	M0	-
Stage 1	T1	N0	M0	A
	T2	N0	M0	B1
Stage 11	T3	N0	M0	B2
	T4	N0	M0	B2
Stage 111	T1, T2,	N1 or N2	M0	C1
	T3, T4	N1 or N2	M0	C2
Stage 1V	Any T	Any N	M1	D

(Cited in Effective Health Care 2004)

Appendix 7

"What is a family history of Bowel Cancer?" – leaflet

At your appointment, you will also be given advice on other family members 'at risk'.

What should I do if I am concerned about my family history and my GP will not refer me to clinical genetics?

This is rare. However, if this does happen please contact the numbers on the back page and you will be given advice by a cancer genetic counsellor.

It is also appropriate for a colorectal nurse, stoma care nurse or practice nurse to refer you to the cancer genetic service, contact details are on the back of this leaflet.

If you share this leaflet with a relative living in Scotland, they can be referred to the nearest Genetic Centre.

Contact Information

There are 4 Genetic Centres in Scotland. Glasgow, Edinburgh, Aberdeen, and Dundee.

West of Scotland Cancer Genetic Service
Ferguson-Smith Centre
Yorkhill Hospital
Dalnair Street
Glasgow
G3 8SJ
Tel: 0141 201 0808

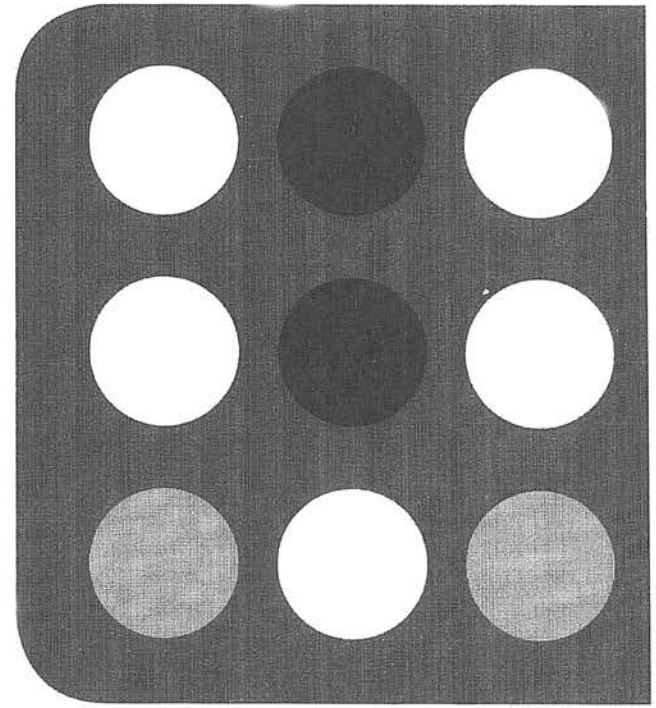
North of Scotland Regional Genetics Service
Department of Medical Genetics
Medical School
Foresterhill
Aberdeen AB9 2ZD
Tel: 01224 552120

Regional Genetics Services
Human Genetics Laboratories
Department of Pathology
Ninewells Hospital and Medical School
Dundee DD1 9SY
Tel: 01382 632680

South East Scotland Clinical Genetics Service
Department of Clinical Genetics
Molecular Medicine Centre
Western General Hospital
Crewe Road South
Edinburgh EH4 2XU
Tel: 0131 651 1012

What is a family history of **bowel cancer?**

Bowel cancer is also known as colorectal colon or rectal cancer



The guidelines in this leaflet apply only to Scotland.

Written by
Roseanne Cetnarskyj BSc (SPQ) RGN
Genetic Nurse Specialist
Edinburgh

NHS
Greater Glasgow

What is cancer genetics?

Cancer genetics is the study of families where an adult has developed cancer at a young age or where there are several members with associated cancers. Research has provided us with the knowledge that some individuals are at an increased risk of developing a cancer when there is a known gene change in their family.

For these families screening and/or testing may be available for those individuals with a family history of cancer, such as, bowel (colorectal), breast and ovarian cancer.

It is known that the same gene can be responsible for increasing the risk of different cancers in a family. For example, bowel and endometrial cancer may be seen in the same family.

This leaflet contains information for those people who wonder if they have a family history of bowel cancer.

A family history of cancer is:

Having a first-degree relative[1], diagnosed with cancer, at a younger age than would normally seen in the population.

[1] 1st degree relatives:
Mother, father, brother, sister or children

A family history can also include; having many relatives with the same or linked cancer, who are first-degree relatives to each other. However, at least one should be **your** first degree relative.

How do I know if I have a family history of bowel cancer?

In Scotland, there are guidelines to help GP's know when to refer a person to a cancer genetic clinic.

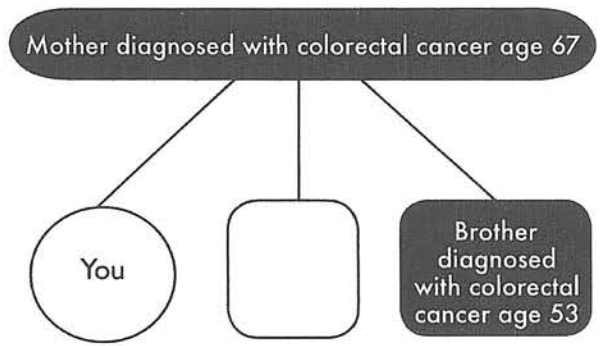
The guidelines below are basic guidance and should be used to help you discuss your family history with your GP.

*One 1st degree relative diagnosed with bowel cancer under age 45.

*Two relatives diagnosed with bowel cancer (one diagnosed under 55) and who are 1st degree to each other and one is 1st degree to you.

*Three relatives diagnosed with bowel cancer, (one may have endometrial or womb cancer), which are 1st degree to each other and one must be 1st degree to you.

Example of a family history that should be referred to a cancer genetic clinic.



What should I do if I think I have a family history of bowel cancer?

Discuss your concerns with your GP. This leaflet may help refresh his/her memory of the guidelines. The address for the GP to make a referral is on the reverse of this leaflet.

What happens if I do go to a cancer genetic clinic?

Your family history will be taken and a pedigree drawn.

Your risk will be assessed and according to your risk assessment, screening by colonoscopy will be discussed. If you are eligible, a referral will be made for you to have a colonoscopy.

If appropriate, genetic testing is discussed. Testing can only be offered if there is a relative alive with bowel or endometrial cancer.

Only a very small number of cancers (approx 5-10%) are caused by a gene change, inherited from a parent at birth. Inheriting a cancer gene change gives you a greater chance of developing cancer than someone who does not have the gene change. However, it **does not mean** that you will definitely get cancer. This will be explained to you at the genetic clinic.

Screening by colonoscopy aims to prevent bowel cancer happening.

Appendix 8

Non-participation form

MRC SCOTTISH COLORECTAL CANCER STUDY

Patients **NOT** taking part in the study

Office Use	Sex	Age	Hospital	Consultant's name	Date invited to take part	Health Board area of residence	Reason for not taking part (if given)
	M / F						CANNOT / DO NOT WANT TO Had surgery? YES / NO CURATIVE / PALLIATIVE
Additional Information(if any)							
	M / F						CANNOT / DO NOT WANT TO Had surgery? YES / NO CURATIVE / PALLIATIVE
Additional Information(if any)							
	M / F						CANNOT / DO NOT WANT TO Had surgery? YES / NO CURATIVE / PALLIATIVE
Additional Information(if any)							

Nurse's Name: ..... Date: .....

Please return to Study Office at the end of each month.

Appendix 9

Family History Recording form

KEY

..... 

..... 

..... 

Case Name..... .....

Date.....

Hospital recruited from.....

Apply label here

I give permission for this information to be used for other members of my family

.....

TDT: yes/no/not eligible

SIBS only: yes/no/not eligible

Appendix 10

Symptom Interview

MRC SCOTTISH COLORECTAL CANCER STUDY
CASE SYMPTOM INTERVIEW

Case ID ☐☐☐☐

It is important to us to hear about your symptoms and your experience before your diagnosis.

☐ Elective ☐ Emergency ☐ FOB Study

1. Which symptom prompted you to discuss it with your GP?

☐ Mth ☐☐ Yr ☐☐

2. Was this the reason you visited your GP? ☐ Yes ☐ No

2a. If NO, did it come up in an appointment for another reason?

☐ Yes ☐ No Comments

3. What did your GP think about your symptoms on this visit?

Please mark with an 'X' what the patient feels was the FIRST SYMPTOM to appear First symptom (Office use) ☐

	Before you went to your GP / had FOB test / or were admitted as an emergency, did you have any of the following symptoms:		How long did you have symptoms before you discussed with GP? **ENTER No. of DAYS ONLY**
4.	Change of bowel habit?	☐ Yes ☐ No	☐
a.	**If YES**, frequency?	☐ Inc ☐ Dec ☐ Both	☐
b.	Increased - no. motions daily?	☐	
c.	Decreased - no. days with NO motion?	☐	
d.	Consistency? **L**ooser/**H**arder	☐ L ☐ H	☐
e.	Timing? **P**ersistent/**I**ntermittent	☐ P ☐ I	☐
f.	Normal habit, per day? ☐ Once ☐ Twice ☐ More than twice	Other? (Specify) ☐	
g.	Rectal Bleeding?	☐ Yes ☐ No	☐
h.	Weight loss?	☐ Yes ☐ No	☐
i.	Loss of energy/ tiredness?	☐ Yes ☐ No	☐

Section 4 continued

	Before you went to your GP / had FOB test / or were admitted as an emergency, did you have any of the following symptoms:	How long did you have symptoms before you discussed with GP? ENTER No. of DAYS ONLY
Excess wind & bloating?	☐ Yes ☐ No	
Loss of appetite?	☐ Yes ☐ No	
Mucus in stools?	☐ Yes ☐ No	
Tenismus?	☐ Yes ☐ No	
Abdominal discomfort?	☐ Yes ☐ No	
Please specify site		
(i) Was it associated with eating?	☐ Yes ☐ No	
(ii) Was it every time you ate?	☐ Yes ☐ No	
Pain?	☐ Yes ☐ No	
Please specify site		
(i) Was it associated with eating?	☐ Yes ☐ No	
(ii) Was it every time you ate?	☐ Yes ☐ No	
Any other symptoms?	☐ Yes ☐ No	
Please specify		
Nausea?	☐ Yes ☐ No	
(i) Was it associated with eating?	☐ Yes ☐ No	
(ii) Was it every time you ate?	☐ Yes ☐ No	
Vomiting?	☐ Yes ☐ No	
(i) Was it associated with eating?	☐ Yes ☐ No	
(ii) Was it every time you ate?	☐ Yes ☐ No	

	After visit to GP & before hospital appointment did you develop any of these symptoms?	How long didyou have any new symptoms before your hospital appointment? ENTER No. of DAYS ONLY	Did you report your new symptoms to your GP?
			☐ N/A
	Change of bowel habit? ☐ Yes ☐ No		☐ Yes ☐ No
a.	**If YES**, frequency? ☐ Inc ☐ Dec ☐ Both		☐ Yes ☐ No
b.	Increased - no. motions daily?		☐ Yes ☐ No
c.	Decreased - no. days with NO motion?		☐ Yes ☐ No
d.	Consistency? **L**ooser/**H**arder ☐ L ☐ H		☐ Yes ☐ No
e.	Timing? **P**ersistent/**E**pisodic ☐ P ☐ I		☐ Yes ☐ No
f.	Normal habit, per day? ☐ Once ☐ Twice ☐ More than twice	Other? (Specify)	
g.	Rectal Bleeding? ☐ Yes ☐ No		☐ Yes ☐ No
h.	Weight loss? ☐ Yes ☐ No		☐ Yes ☐ No
i.	Loss of energy/ tiredness? ☐ Yes ☐ No		☐ Yes ☐ No
j.	Excess wind & bloating? ☐ Yes ☐ No		☐ Yes ☐ No
k.	Loss of appetite? ☐ Yes ☐ No		☐ Yes ☐ No
l.	Mucus in stools? ☐ Yes ☐ No		☐ Yes ☐ No
m.	Tenismus? ☐ Yes ☐ No		☐ Yes ☐ No
n.	Abdominal discomfort? ☐ Yes ☐ No		☐ Yes ☐ No
o.	Please specify site		
	(i) Was it associated with eating? ☐ Yes ☐ No		☐ Yes ☐ No
	(ii) Was it every time you ate? ☐ Yes ☐ No		☐ Yes ☐ No
p.	Pain? ☐ Yes ☐ No		☐ Yes ☐ No
q.	Please specify site		
	(i) Was it associated with eating? ☐ Yes ☐ No		☐ Yes ☐ No
	(ii) Was it every time you ate? ☐ Yes ☐ No		☐ Yes ☐ No

	After visit to GP & before hospital appointment did you develop any of these symptoms?	How long didyou have any new symptoms before your hospital appointment? ENTER No. of DAYS ONLY	Did you report your new symptoms to your GP?
Any other symptoms?	☐ Yes ☐ No		☐ Yes ☐ No
Please specify			
Nausea?	☐ Yes ☐ No		☐ Yes ☐ No
(i) Was it associated with eating?	☐ Yes ☐ No		☐ Yes ☐ No
(ii) Was it every time you ate?	☐ Yes ☐ No		☐ Yes ☐ No
Vomiting?	☐ Yes ☐ No		☐ Yes ☐ No
(i) Was it associated with eating?	☐ Yes ☐ No		☐ Yes ☐ No
(ii) Was it every time you ate?	☐ Yes ☐ No		☐ Yes ☐ No

If you had bleeding when going to the toilet, was it? (Tick all that apply) ☐ N/A

☐ Bright red ☐ Dark red ☐ Mixed in stool ☐ Coating stool ☐ On toilet paper ☐ Large volume

5a. Did you experience any symptoms in your bottom (anal region)? ☐ Yes ☐ No

If **YES**, which of the following? (Tick all that apply)

☐ Soreness ☐ Itching ☐ Lumps ☐ Discomfort ☐ Pain ☐ Prolapse

Did you self medicate for any of these symptoms before visiting your GP? ☐ Yes ☐ No

If **YES**, which symptoms?

For how long?

Before visiting your GP, did you talk to anyone about your symptoms? ☐ Yes ☐ No

If **YES**, who did you speak to?

IF THERE WERE SYMPTOMS OF ANY KIND FOR 4 WEEKS OR MORE, ASK QUESTION 7

Was there a reason you waited with your symptoms to visit your GP? ☐ N/A

Reason?

After telling your GP about your symptoms did you have any of the following:

8a. Request for sample of stool? ☐ Yes ☐ No

If **YES**, was it tested

i) For blood? ☐ Yes ☐ No ☐ Don't know

ii) For infection? ☐ Yes ☐ No ☐ Don't know

iii) Were you given the result? ☐ Yes ☐ No

If you were given the result, what did the GP say to you?

8b. Rectal examination? ☐ Yes ☐ No

If **YES**, what did the GP say ?

If **NO** at first visit, did you have a rectal examination from GP at any time before hospital appointment? ☐ Yes ☐ No

Result?

8c. Abdominal examination? ☐ Yes ☐ No

What did GP say?

8d. Blood test? ☐ Yes ☐ No

If **YES**, what results were you given?

How many times did you visit your GP with any of the symptoms before you were referred to the hospital?

☐ Once ☐ 2 or 3 times ☐ 4 or 5 times ☐ > 5 times

10. **Before** your diagnosis, when you went to the toilet did you:

Look at the contents of the toilet **before you flushed it**? ☐ Yes ☐ No

If **YES**, how often?

10a. ☐ Every time ☐ Once a week ☐ Once a month ☐ Sometimes ☐ Never

10b. Look at the toilet paper? ☐ Yes ☐ No

If **YES**, how often?

10c. ☐ Every time ☐ Once a week ☐ Once a month ☐ Sometimes ☐ Never

11. **Before** your diagnosis, how would you describe your knowledge of bowel (colorectal) cancer symptoms?

☐ None ☐ A little ☐ Good ☐ Very good ☐ Expert

2. **Before** your diagnosis, did you consider the possibility of having cancer? ☐ Yes ☐ No

If **YES**, when did you first think this: (TICK ONLY ONE BOX)

Before visit to GP? ☐

After tests? ☐

On referral to hospital? ☐

Other? ☐ Specify

If **NO**, what did you think was wrong?

3. Would you say you have a family history of colorectal cancer? ☐ Yes ☐ No ☐ Don't know

13a. Would you say you have a family history of cancer? ☐ Yes ☐ No ☐ Don't know

If **YES,**

13b. Have you ever discussed this with your GP? ☐ Yes ☐ No

Were you referred to a genetic department? ☐ Yes ☐ No

4. In the **past two years** have you had any other admissions to hospital? ☐ Yes ☐ No

If **YES**, please give details:

Reason for admission?

Mth ☐☐ Yr ☐☐ Did you have surgery? ☐ Yes ☐ No

Please give details

Reason for admission?

Mth ☐☐ Yr ☐☐ Did you have surgery? ☐ Yes ☐ No

Please give details

Reason for admission?

Mth ☐☐ Yr ☐☐ Did you have surgery? ☐ Yes ☐ No

Please give details

Appendix 11

Consent to access Medical Records

MRC
Medical Research Council

MRC Scottish Colorectal Cancer Study

Consent for Access to Medical Notes

Name _____

Date of Birth _____

Address _____

_____

Postcode _____

I give permission for my medical notes and information from them to be released to the Principal Investigators and the research staff of the Scottish Colorectal team.

I also give permission to photocopy all or any reports and/or notes relevant to my case, including access to clinical information held on electronic format and databases.

This permission is extended to duration time of the study. My notes may be requested on several occasions during this study.

Signed ..... Date .....

study id number:

Appendix 12

Medical Extraction form with Charlson Comorbidity Index

Medical Record Extraction Form and Comorbidity Index

Case ID	«CaseID»

1. Is there a referral letter? ☐ Yes ☐ No ☐ FOB Study

2. If No, date of first letter? ☐☐/☐☐/20☐☐

3. If Yes, who from? ☐

4. Type of referral? Routine ☐
   Urgent ☐
   Not indicated ☐

5. Date of referral letter? ☐☐/☐☐/20☐☐

6. Who was referral letter to?
   Surgeon ☐
   Physician ☐
   Open access ☐
   Other ☐
   Please specify ☐

7. Did referral letter or first letter indicate diagnosis? ☐ Yes ☐ No

8. If Yes, what was it? ☐

9. Admission? Elective ☐
   Emergency ☐

10. If emergency, what for? Pain ☐
    Bleeding ☐
    Perforation ☐
    Obstruction ☐
    Blood transfusion ☐
    Other ☐
    Please specify, Other (1) ☐
    Other (2) ☐

11. Any symptoms indicated on referral letter or first letter? ☐ Yes ☐ No ☐ N/A ☐ On admission

12. If Yes, what were they? *(Tick all which apply)*

Constipation?	☐	Diarrhoea?	☐
Loose stools?	☐	Change in bowel habit?	☐
Rectal bleeding?	☐	More frequent stools?	☐
Intermittent diarrhoea and constipation?	☐		
Weight loss?	☐	Loss of energy/tiredness?	☐
Loss of appetite?	☐	Excess wind and bloating?	☐
Mucus in stool?	☐	Vomiting?	☐
Nausea?	☐	Palpable abdominal mass?	☐
Abdominal pain?	☐	Abdominal discomfort?	☐
If Yes, location of abdominal pain	☐ Right	If Yes, location of abdominal discomfort	☐ Right
	☐ Left		☐ Left
	☐ Central		☐ Central
	☐ Not recorded		☐ Not recorded
Other?	☐		
Please specify			

13. Were any tests carried out by GP before referral or at open access clinic? ☐ Yes ☐ No ☐ Don't know

14. If Yes, what were they?

15. Date 1st appointment at hospital ☐☐/☐☐/20☐☐

16. What was the appointment for?

17. Investigations in hospital prior to surgery:

None ☐

Flexible Sigmoidoscopy ☐

Rigid Sigmoidoscopy ☐

Sigmoidoscopy ☐

Colonoscopy ☐

Barium Enema ☐

Abdominal Ultrasound ☐

Endorectal Ultrasound ☐

Chest Xray ☐

Abdominal Xray ☐

Abdominal CT scan ☐

Pelvic CT Scan ☐

Other? ☐

Please specify ☐

18. Surgery? ☐ Yes ☐ No

Date of surgery? ☐☐/☐☐/20☐☐

If no surgery, date of pathology? ☐☐/☐☐/20☐☐ **Office use only**

19. Duke's Staging? **(1)** **(Circle)** **A** **B** **C** **C1** **C2** **D** **N/A**

Tumour (T) **1** **2** **3** **4**

Nodes (N) ☐ Yes ☐ No

Metasteses (M) ☐ Yes ☐ No

Duke's Staging? **(2)** **(Circle)** **A** **B** **C** **C1** **C2** **D** **N/A**

Tumour (T) **1** **2** **3** **4**

Nodes (N) ☐ Yes ☐ No

Metasteses (M) ☐ Yes ☐ No

20. Earliest Hb recording? (Date) ☐☐/☐☐/20☐☐

21. Result? ☐

22. Site of Tumour ?

- Ceacal Valve ☐
- Splenic Flexure ☐
- Transverse Colon ☐
- Rectum ☐
- Caecum ☐
- Rectosigmoid ☐
- Sigmoid ☐
- Anus ☐
- Appendix ☐
- Other ☐

Details of other site? ☐

23. Operation?

- R Hemi ☐
- L Hemi ☐
- Sigmoid Colectomy ☐
- Total Colectomy ☐
- SubTotal Colectomy ☐
- Anterior Resection ☐
- Limited Resection ☐
- Recto-Sigmoid Resection ☐
- Colorectal Resection ☐
- APR ☐
- Hartmann's ☐
- Bypass ☐
- Panproctocolectomy ☐
- Polypectomy ☐
- Transanal Excision ☐
- Local Excision of Rectal Tumour ☐
- Total Mesorectal Excision of Rectum ☐

Defunctioning Colostomy ☐

Inoperable ☐

No Surgery ☐

24. Reason for operation? Curative ☐

Palliative ☐

25. Was there anastomotic leak? ☐ Yes ☐ No ☐ Don't know

26. Was tumour fixed? ☐ Yes ☐ No ☐ Don't know

27. If Yes, was adjacent organ resectioned? ☐ Yes ☐ No ☐ Don't know

28. If Yes, which organs? ☐

29. Comorbidity ASA **(Circle)** **1** **2** **3** **4** **N/A**

30. Date of death if applicable? ☐☐/☐☐/2☐☐☐

Continued

Comorbidity Index

Case ID	«CaseID»

Tick box if recorded in notes			
Myocardial		Charlson weighted score	
Angina			
Arrhythmia			
Valvular			
Myocardial infarction			
Congestive heart failure			
Vascular			
Hypertension			
Peripheral vascular			
Cerebrovascular			
Pulmonary			
Mild			
Severe-moderate			
Neurological			
Dementia			
Hemiplegia(para)			
Other neurological			
Endocrine			
Diabetes			
Diabetes with end organ			
Other endocrine			
Renal			
Mild insufficiency			
Moderate to severe			
Liver			
Mild			
Moderate to severe			
Gastrointestinal			
GI bleeding			
Inflammatory bowel			
Peptic ulcer			
Cancer/immune			
Tumour			
Lymphoma			
Leukaemia			
Aids			
Metastatic cancer			
Miscellaneous			
Rheumatologic			
Coagulopathy			
Others			
		Total Score	

Comments:

Appendix 13

Satisfaction Study Report

Assessment of participants views on consent procedures

We carried out a cross sectional postal questionnaire survey (questionnaire attached on CD) among SOCCS participants from three defined regions. We approached 120 cases and 117 controls with an invitation to take part. The survey received local ethical research committee approval. Responses were received from 157 (66%) participants. A full report is available should this be desired. In summary:-

Response rates were slightly higher in younger age groups and among participants who took part in the SOCCS study in the past 12 months. Otherwise there were no statistically significant differences between responders and non-responders.

Information sheet

92% thought the detail in the information sheet was "just right"; 5% thought it "too detailed" and 3% "not detailed enough"

91% thought that is was completely clear and easy to understand

72% found it "very helpful", 23% "quite helpful" and 5% "not helpful" in helping to decide whether to participate. Some (10/42) of those who did not find it very helpful noted that this was because they had already decided to take part.

Many aspects of the information sheet were considered to be important by >90% of the respondents. Aspects which seemed least important were:

- Who else is participating (noted by only 45%)
- Who funded the study (noted by 52%)

Consent form (which followed the MRC template and required multiple aspects to be consented to individually

96% of respondents did not find the consent form too complicated. Despite this 84% noted that they would have preferred to have given a single general consent to take part to all aspects noted in the information sheet and consent form. There was a trend for a lower proportion to prefer this option with increasing time since recruitment to the study, suggesting that views on this change over time.

97% felt they had sufficient time to read through the consent form. However, 77% would have preferred the consent form to be mailed to them prior to seeing the nurse.

52% noted that they decided to take part immediately, 27% after a few hours and 21% after a day or more. Cases took less time to decide to take part than controls. Younger and respondents and those from less deprived areas also took less time to decide to take part.

Role of interview with the research nurse

77% of respondents felt that this was a necessary part of the consent process. 75 (63%) respondents gave reasons for this opinion. The most commonly stated reason

was that it aided understanding and gave opportunity to clarify points. Feeling on this issue was quite strong, particularly among cases. An illustrative quote is *"the interview helped me to clarify and reinforce the reasons for the study"*

Reasons for taking part

The most common categories of reasons were:

results may improve treatments for future sufferers of bowel cancer	88%
to contribute towards medical research	79%
just wanted to help	68%

Appendix 14

Sample Genetic Referral Proforma

Family History Ascertainment Form

To help you ascertain if this patient needs a referral to cancer genetic services. Please ask the following questions

CIRCLE AS APPROPRIATE

Have you ever had a diagnosis of cancer? YES NO

Have any of your children ever had a diagnosis of cancer? YES NO

Have any of your brothers or sisters ever had a diagnosis of cancer? YES NO

Has your mother ever had a diagnosis of cancer? YES NO

Has your father ever had a diagnosis of cancer? YES NO

Only complete if one or more answers are YES.

Site of cancer				
Sex				
Age at diagnosis				
Relationship to patient				
Comments				

Use reverse for more details

At least **one** first-degree relative with colorectal cancer diagnosed **under age 45**
Or
Two relatives with colorectal cancer that are first-degree to each other **and one** diagnosed **under age 55.**
Or
Several relatives with cancer including; colorectal cancer, ovarian or endometrial cancer.
Or
Many varied cancers (excluding lung cancer and cervical cancer)

Patients meeting any one of the above criteria please refer patient to cancer genetics and give a leaflet to patient about the cancer genetic services.

Sent referral to clinical genetics on Date .....

Information leaflet on family history and cancer genetic services given YES NO

Please apply patient ID label.

Copy should be filed in medical

Appendix 15

Sample Urgent Referral Proforma for Patients with lower gastrointestinal symptoms meeting high-risk criteria

Urgent referral form for suspected colorectal cancer

Name.....

Address.....

Postcode..... Telephone number .....

D.O.B.....

I would like this patient of mine to be sent an urgent appointment.
Mr..... does /does not meet the criteria for urgent referral.

Symptom referral guidelines

	Age	Tick box or boxes for this patient
Rectal bleeding WITH a change in bowel habit to looser stools and/or increased frequency of defecation persistent for 6 weeks	*All ages*	
A definite palpable right-sided abdominal mass.	*All ages*	
A definite palpable rectal (not pelvic) mass	*All ages*	
Rectal bleeding persistently **WITHOUT** anal symptoms	*Over 50 yrs*	
Change of bowel habit to looser stools and/or increased frequency of defecation, **WITHOUT** rectal bleeding and persistent for six weeks.	*Over 60 yrs*	
Iron deficiency anaemia **WITHOUT** an obvious cause (Hb < 11 g/dl in men or < 10 g/dl in postmenopausal women).		

Circle as appropriate

I have carried out a rectal examination Yes No

Findings

I have carried out an abdominal examination Yes No

Findings (including location of mass)

I have checked Haemoglobin levels Yes No

Result

Comments and family history on reverse Yes No

Please record reason for patient to be seen URGENTLY, if they do not meet the referral guidelines.

Please give any further information you feel is necessary for the care of this patient.
Please record family history of colorectal cancer in family. Note relationship to your patient and age at diagnosis.

Comments

GP stamp